(12)

AD-A181 549

USAFSAM-TR-85-99

THE EFFECTS ON PILOT PERFORMANCE OF ANTIEMETIC DRUGS ADMINISTERED SINGLY AND IN COMBINATION

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March 1987

Final Report for Period February 1983 - May 1985

Prepared for

USAF SCHOOL OF AEROSPACE MEDICINE
Human Systems Division (AFSC)
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NOTICES

This final report was submitted by the University of Illincis, Aviation Research Laboratory, Willard Airport, Savoy IL 61874, under contract F33615-83-K-0612, job order 7757-05-60, with the USAF School of Aerospace Medicine, Human Systems Division, AFSC, Brooks Air Force Base, Texas. Dr Thomas G. Wheeler (USAFSAM/RZV) was the Laboratory Project Scientist-in-Charge.

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The Office of Public Affairs has reviewed this report, and it is releasable to the National Technical Information Service, where it will be available to the general public, including foreign nationals.

This report has been reviewed and is approved for publication.

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UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

AD-A181 549

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution is unlimited.
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S) USAFSAM-TR-85-99
6a. NAME OF PERFORMING ORGANIZATION Institute of Aviation, University of Illinois — 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION USAF School of Aerospace Medicine (RZV)
6c. ADDRESS (City, State and ZIP Code) Willard Airport Savoy, IL 61874	7b. ADDRESS (City, State and ZIP Code) Human Systems Division (AFSC) Brooks Air Force Base, TX 78235-5301
8a. NAME OF FUNDING/SPONSORING ORGANIZATION — 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER F33615-83-K-0612
8c. ADDRESS (City, State and ZIP Code)	10. SOURCE OF FUNDING NOS. PROGRAM ELEMENT NO. 62202F — PROJECT NO. 7757 — TASK NO. 05 — WORK UNIT NO. 60

11. TITLE (Include Security Classification)
THE EFFECTS ON PILOT PERFORMANCE OF ANTIEMETIC DRUGS ADMINISTERED SINGLY AND IN COMBINATION

12. PERSONAL AUTHOR(S) Taylor, Henry L.; Dellinger, John A.; Weller, Martha H.; Richardson, Bruce C.; Hyman, Fred C.; LeGrand, James E.; Domino, Edward F.; and Nagel, Robert J.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Yr., Mo., Day)	15. PAGE COUNT
Final Report	FROM Feb 1983 TO May 1985	1987, March	100

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB. GR.	Emesis, Performance, Drug Effects
06	16		
06	15		

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Four experiments were conducted to evaluate the effects on human performance of alcohol and antiemetic drugs. In Experiment I, the effects on pilot performance of 4 blood alcohol levels (BAL) were investigated to determine the sensitivity of the methodology. Experiment II evaluated the effects on pilot performance in a flight simulator of prescribed dosages of thiethylperazine (10 mg), promethazine hydrochloride (25 mg), cimetidine (300 mg), and a placebo control. The 3 drugs and the placebo were administered to 16 male subjects. Two tasks, a two-dimensional tracking task which is part of an instrument landing system (ILS) approach and the Sternberg Memory Search task, were used to generate pilot performance data. A Latin square design was used to balance treatment order effects, and each subject received each treatment condition. Log root mean square (RMS) deviation values, computed

cont'd over

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT ☐ DTIC USERS ☐	21. ABSTRACT SECURITY CLASSIFICATION Unclassified
22a. NAME OF RESPONSIBLE INDIVIDUAL Thomas G. Wheeler, Ph.D.	22b. TELEPHONE NUMBER (Include Area Code) (512) 536-3685 — 22c. OFFICE SYMBOL USAFSAM/RZV

DD FORM 1473, 83 APR — EDITION OF 1 JAN 73 IS OBSOLETE.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

19. ABSTRACT (Continued)

from the simulator flight data (altitude straight and level, altitude turning, localizer and glide slope tracking) were used to test the main effects. The results indicated a significant drug effect. Univariate analyses resulted in a significant drug main effect on 2 primary task variables--altitude straight and level, and localizer tracking. The contrasts between promethazine hydrochloride and the control were significant for altitude straight and level and for glide slope tracking. The other contrasts were not significant except for the control-thiethylperazine contrast for the localizer tracking variable. For this variable, performance for the thiethylperazine condition was better than for the control condition. Another study has indicated that when the 3 drugs were administered singly to dogs, only thiethylperazine effectively increased the radiation threshold compared to a control group. In experiment II, thiethylperazine produced no significant performance effects. These results suggest that thiethylperazine should be used if a single drug is to be administered to prevent radiation-induced emesis in aircrews.

contd

In Experiment III the effects of combinations of antiemetic drugs were investigated. Two additional flight task dependent variables, turning rate control while straight and level and while turning, were added.) The results indicated a significant drug effect due to the promethazine hydrochloride, thiethylperazine and cimetidine (PTC) combination. The thiethylperazine and cimetidine (TC) combination produced no performance deficits. These results indicate that the TC combination can be used without flight performance degradation. While the PTC offers the greatest protection against emesis (7% over TC), there is a significant performance decrement associated with the PTC combination. The results indicate that the TC combination should be used if drugs are to be administered to prevent radiation-induced emesis in aircrews.

Experiment IV evaluated the effects of alcohol on pilot performance; the results were compared with the performance degradations resulting from combinations of antiemetic drugs. The results indicated that 0.12% BAL produced a decrement in pilot simulator instrument flight performance. In comparison with the PTC effects, the high BAL produced a relatively larger performance decrement than the PTC combination. Keywords: flight simulation; Pilot studies; intoxication

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Justification

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Distribution/
Availability Codes

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INTRODUCTION

Exposure to high levels of ionizing radiation produces nausea and emesis in humans and in nonhuman primates, pigs, cats, and dogs (1). Clinically, physicians have treated this nausea-emesis syndrome with a variety of drugs including phenothiazines (2). Marks (3) reported the use of chlorpromazine to treat radiation sickness. For some time, the USAF School of Aerospace Medicine has been interested in the problem of inhibition of radiation-induced emesis since military personnel may have to perform critical jobs in spite of exposure to radiation (4). The U.S. Air Force is particularly interested in the performance capability of aircrews in the event of radiation exposure.

Gralla et al. (5) used young male beagle dogs to investigate the effects of drug inhibition of first-stage radioemesis. Of seven drugs tested, they found that chlorpromazine was the most effective in inhibiting first-stage emesis. The use of a phenothiazine such as chlorpromazine to inhibit emesis appears to be contraindicated for military personnel due to potential performance decrements caused by the drug. To test the ability of specific drugs to inhibit emesis in dogs, Cooper and Mattsson (6) selected the following off-the-shelf drugs: thiethylperazine, promethazine hydrochloride, cimetidine, and naloxone. Thiethylperazine is a phenothiazine; promethazine hydrochloride is a phenothiazine derivative; cimetidine is a histamine H_2 receptor antagonist; and naloxone is a narcotic antagonist. They found that thiethylperazine, promethazine hydrochloride, and cimetidine all significantly increased the radiation threshold for emesis, but the threshold in dogs treated with naloxone was not significantly different from the controls. They reported that promethazine hydrochloride (2 mg/kg) increased the ED_{50} for radiation-induced emesis to 402 rad compared to 170 rad in controls. Thiethylperazine (0.86 mg/kg) increased the ED_{50} to 320 rad and cimetidine (4 mg/kg) increased the threshold to 331 rad.

In a second study, designed to further investigate the ED_{50} of radiation-induced emesis, Mattsson et al. (1) administered the same drugs to dogs using only about one-fourth the dose for promethazine hydrochloride (13.9 mg/m^2) and for thiethylperazine (5.57 mg/m^2), but a somewhat higher dose of cimetidine (167 mg/m^2). The three drugs were administered separately and in the following combinations: cimetidine and promethazine hydrochloride; cimetidine and thiethylperazine; promethazine hydrochloride and thiethylperazine; and cimetidine, promethazine hydrochloride, and thiethylperazine. Of the single drugs, only thiethylperazine was statistically more effective ($P<0.5$) compared to the control conditions in increasing the radiation-induced emesis threshold. The following two combinations of antiemetic drugs were more effective than the control condition: thiethylperazine and cimetidine (TC); and promethazine hydrochloride, thiethylperazine, and cimetidine (PTC).

Of the previously mentioned species that experience nausea and emesis after exposure to ionizing radiation, the dog appears to be the best

experimental model for studying the prevention of radiation-induced emesis in humans (1,7). The dog has a radiation-induced emesis threshold similar to the human threshold. Both species have modest plasma histamine activity and both are sensitive to apomorphine (1). Although these similarities between the two species allow conclusions drawn from the emesis threshold data obtained in the dog studies to be applied to a human population, further study is needed to determine if antiemetic drugs that have been shown to inhibit radioemesis in dogs cause significant performance decrements in humans.

Taylor et al. (8) evaluated the effects on pilot performance of these 3 antiemetic drugs administered singly. The commonly prescribed dosages, standardized for a 70 kg person, of thiethylperazine (10 mg), promethazine hydrochloride (25 mg), and cimetidine (300 mg), and a placebo control were administered to 16 male general aviation pilots. Pilot performance on an instrument flight task was evaluated in a flight simulator. Two tasks were used to generate performance data: (1) flying the simulator, which included a two-dimensional tracking task that is part of an instrument landing system (ILS) approach; and (2) the Sternberg Memory Search task. A multivariate analysis of variance (MANOVA) was used to determine the effects of the drugs on 4 performance measures: altitude control straight and level, altitude control turning, ILS localizer (lateral) tracking, and ILS glide slope (GLS) (vertical) tracking. They found that the drug main effect was significant. Further analyses indicated that altitude control straight and level, and ILS localizer tracking had a significant drug main effect, but that the other 2 variables were not significant. Contrasts between promethazine hydrochloride and the control were significant for 2 variables, and between the control and thiethylperazine for 1 variable. The latter contrast was the result of better localizer tracking for the thiethylperazine condition than for the control condition.

An important question to be addressed is the relative significance of performance decrements resulting from the ingestion of antiemetic drugs. Klein (9) proposed that ethyl alcohol could be used as a reference substance for evaluating the relative performance decrements of drugs. The ingestion of ethyl alcohol has been shown to impair pilot performance on instrument flying tasks in simulators (10,11) and in a light aircraft (12). Aksnes (10) concluded that a blood alcohol level (BAL) of about 0.05% impairs a pilot's ability to perform elementary flight maneuvers in a Link Trainer. Henry et al. (11) used pilot performance in a Link General Aviation Trainer (GAT-1) to evaluate the effects of alcohol and other drugs and/or stressors on pilot performance. United States Air Force instructor pilots received 0.3, 0.6, and 0.9 g alcohol/kg body weight, and subsequently performed a series of instrument flight maneuvers. The investigators found statistically significant performance decrements at the measured BALs of approximately 60 and 100 mg percent (equivalent to percent BAL), but not at 30 mg percent.

A methodology, using a digital microprocessor to automatically measure pilot performance in a general aviation flight simulator, has been developed at the Aviation Research Laboratory (ARL), Institute of Aviation (13). The methodology consists of measuring the performance of 2 tasks performed simultaneously. The primary task consists of an instrument flight divided into a holding phase followed by a two-dimensional tracking task which is part of an ILS approach. The secondary task is the Sternberg Memory Search task. For the primary task, root mean square (RMS) deviations have been used to

measure the effects of drugs on pilot performance in the flight simulator (14,15). The RMS computation is similar to computing a standard deviation except that a targeted value is used as the parameter mean. The RMS is generally accepted as the best single measure of error amplitudes (16). The secondary task was included in the methodology since drugs may in fact reduce the pilot's capacity to perform, even though performance on the primary task may remain unchanged from a control condition. Wickens et al. (17) have discussed the Sternberg Memory Search task as a measure of a pilot's residual capacity. For this task, a series of letters known as the memory set (MSET) are presented while the pilot is performing the primary task. A probe letter is subsequently presented and the pilot responds "true" or "false", respectively, depending on his decision of whether the probe was or was not contained in the MSET. The Sternberg Memory Search task (18) assumes a serial, exhaustive scan of the MSET held in working memory. Thus, an MSET of 4 letters should result in a longer reaction time than an MSET of 2 letters.

The laboratory is also interested in evaluating the effects of toxic substances on pilot performance (14,15) and in examining physiological correlates of these effects. Two correlates, heart period (HP) or the beat-to-beat interval, and heart-period variability (HPV) or the change in sequential beat-to-beat intervals over time, have been investigated extensively. It is well known that respiration induces phasic modulation of vagal influence on the heart rate. This component of heart-rate variation is respiratory sinus arrhythmia (RSA). Recently, researchers have sought noninvasive methods for measuring RSA to estimate the vagal influence on the heart. Vagal control of heart rate can be estimated by measuring the mean heart period (MHP) and the heart-period variability associated with the normal respiratory frequency band. The analysis of these variables was used to derive a measure of RSA, $\hat{V}$, which is the representation of the amount of heart-period variance due to respiration (19). Yongue et al. (20) showed, in a free-moving, unanesthetized rat, that $\hat{V}$ was sensitive to manipulations of vagal tone by atropine and phenylephrine. Dellinger (21) and Taylor et al. (22) showed that atropine significantly affects pilot performance as measured in a flight simulator as well as mean heart period, heart-period variance, and $\hat{V}$. Promethazine hydrochloride, a drug that exhibits anticholinergic properties, may also modulate RSA.

This final report covers the results of 4 experiments. The purpose of the first experiment was to evaluate the performance effects of 4 BALs to determine the sensitivity of the methodology used in Experiment II to measure pilot performance effects of the commonly prescribed dosages of promethazine hydrochloride, thiethylperazine, and cimetidine. The first 2 experiments have been reported in detail by Taylor et al. (8), and, for completeness, only the results are included in this report. The purpose of Experiment III was to determine the effects on pilot performance of 2 combinations of antiemetic drugs: (1) thiethylperazine (10 mg) and cimetidine (300 mg); and (2) promethazine hydrochloride (25 mg), thiethylperazine (10 mg), and cimetidine (300 mg). Experiment IV evaluated the effects of 3 BALs on pilot performance to provide a reference for evaluating the relative performance decrements caused by antiemetic drug combinations.

METHOD

Equipment

The equipment used to collect flight performance data for all 4 experiments consisted of a fixed-base flight simulator that was controlled by a single 16-bit computer. The simulator (Fig. 1), referred to as ILLIMAC 2 (an acronym for ILLInois Micro Aviation Computer), was modeled after the ILLIMAC engineering prototype simulator (23). Both the ILLIMAC engineering prototype and the ILLIMAC 2 were designed and developed by ARL personnel at the Institute of Aviation, University of Illinois at Urbana-Champaign. The shell, base, and rudder pedals of a commercially available GAT-1 were used by ARL personnel to construct ILLIMAC 2. The instrumentation, computer, and electronic components were designed and constructed by ARL personnel.

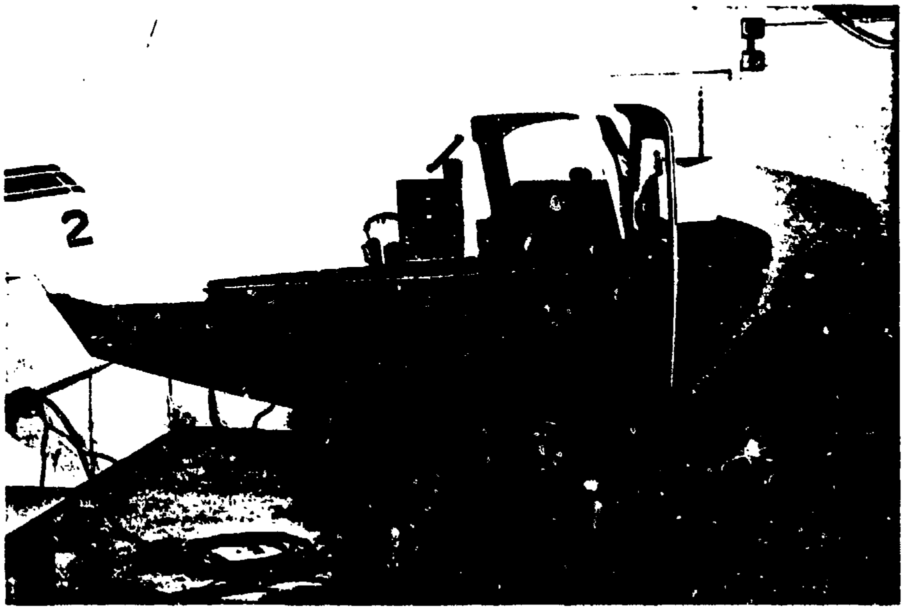

Figure 1. ILLIMAC 2 simulator.

The ILLIMAC 2 computer consists of a microprocessor section, a special function section, and an input/output (I/O) section. The microprocessor section contains an Intel Corporation 8086 chip on the Microprocessor board plus two additional boards: (1) a PROM/RAM board that contains 32K bytes of memory, and (2) an address decode and clock frequencies board. The special function section consists of an array processor board, a trigonometric digital/analog (D/A) board, and a trigonometric look-up tables board. The array processor board enables the single microprocessor to achieve the speed necessary to perform simulation functions at a 30-Hz update rate. The input/output section contains 12 printed circuit boards that control I/O functions between the cockpit and the computer. These boards drive all analog functions in the cockpit, and receive digital and analog information from the cockpit.

The ILLIMAC 2 simulates the flight characteristics of the Piper Lance, a complex, high performance, single-engine aircraft. The ILLIMAC 2 flight panel (Fig. 2) contains the instrumentation and navigation/communication equipment used for instrument flight rules (IFR) flights. Navigational facilities and airports are preprogrammed in the computer. An X-Y flight path recorder (Fig. 3) was used to record horizontal tracings of holding patterns and approaches to the University of Illinois-Willard Airport.

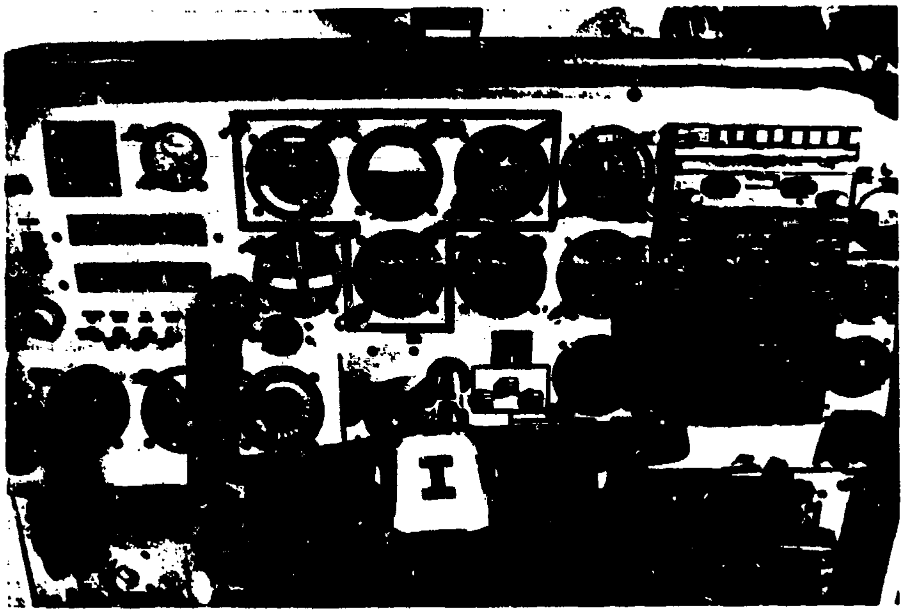

Figure 2. ILLIMAC 2 flight panel.

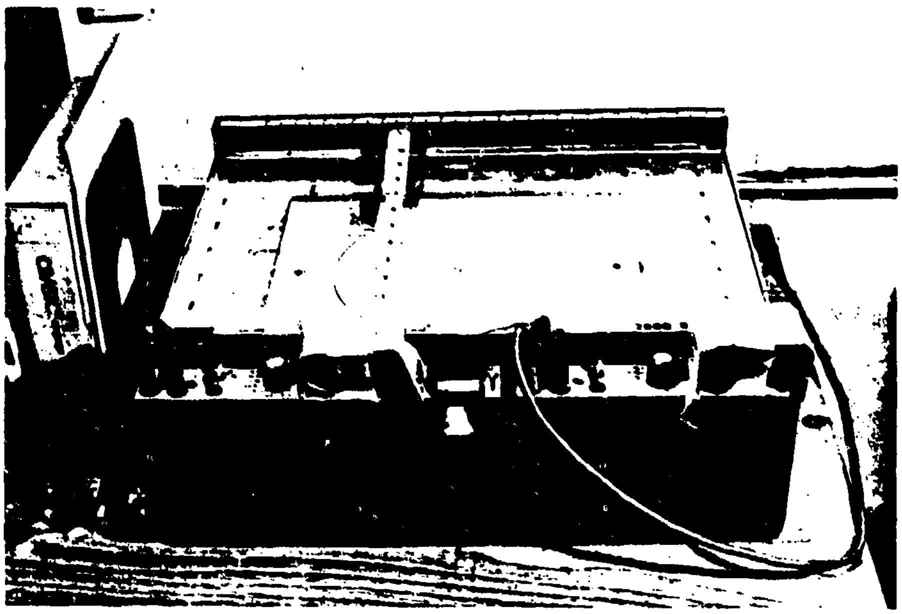

Figure 3. ILLIMAC 2 X-Y flight path recorder.

A CompuPro 8086 computer, with two 8-in. floppy disk drives and a cathode-ray tube (CRT) (Fig. 4), connected serially to the ILLIMAC 2 was used to record digital performance data generated during flight. The CompuPro drove a speech synthesizer (Netronics, Inc., New Milford, Conn., Electric Mouth, VOX II) which generated and presented auditory stimuli to the ILLIMAC cockpit.

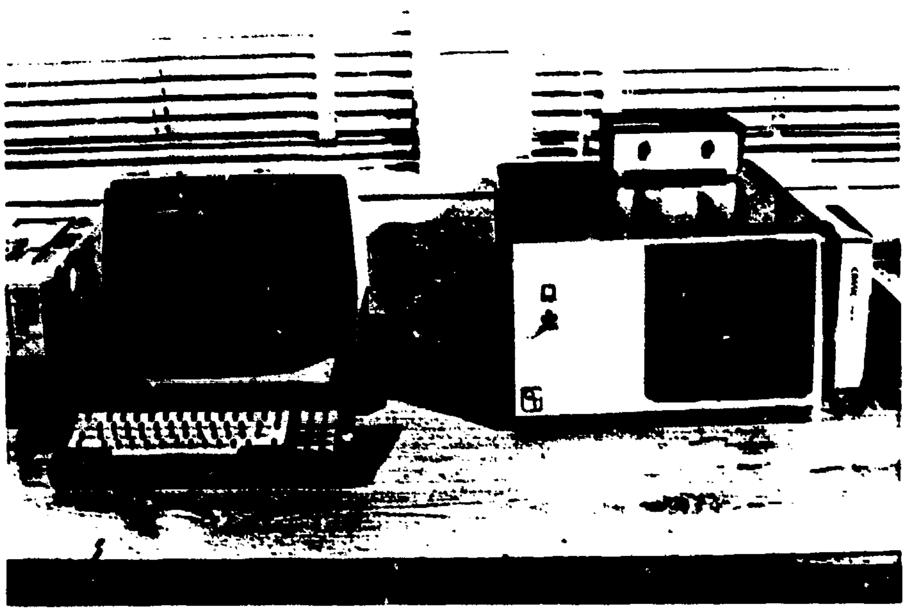

Figure 4. CompuPro 8086 computer.

A Smith and Wesson Electronics Company Breathalyzer Model 1000 was used to estimate BALs from breath samples for Experiments I and IV. During Experiment II, a thoracic expansion belt was used to record respiratory cycles. Heart electrical potentials were transmitted through 3 Beckman biopotential silver-silver chloride electrodes to a Beckman Type RD Dynograph Recorder (Fig. 5) that in turn amplified the signal and relayed it for recording to a Hewlett-Packard Model 3960 FM tape recorder.

Subjects

Each subject in all 4 experiments signed a consent form approved by the University of Illinois Institutional Review Board and received a preexperimental physical including an electrocardiogram (ECG). Each subject was scheduled for a post-experimental physical.

Experiment I. Eight male general aviation pilots ranging in age from 21 to 23 years of age were used as subjects for Experiment I. With the exception of 1 subject, minimum flight experience was 150 h; flight experience ranged from 105 to 460 h with a mean time of 275 h. Simulator experience ranged from 28 to 57 h with a mean time of 40 h. A problem drinker questionnaire was used to select light-to-moderate drinkers with no histories of alcohol abuse (24).

Experiment II. Sixteen male general aviation pilots ranging in age from 19 to 32 years of age were used as subjects. The minimum flight experience of

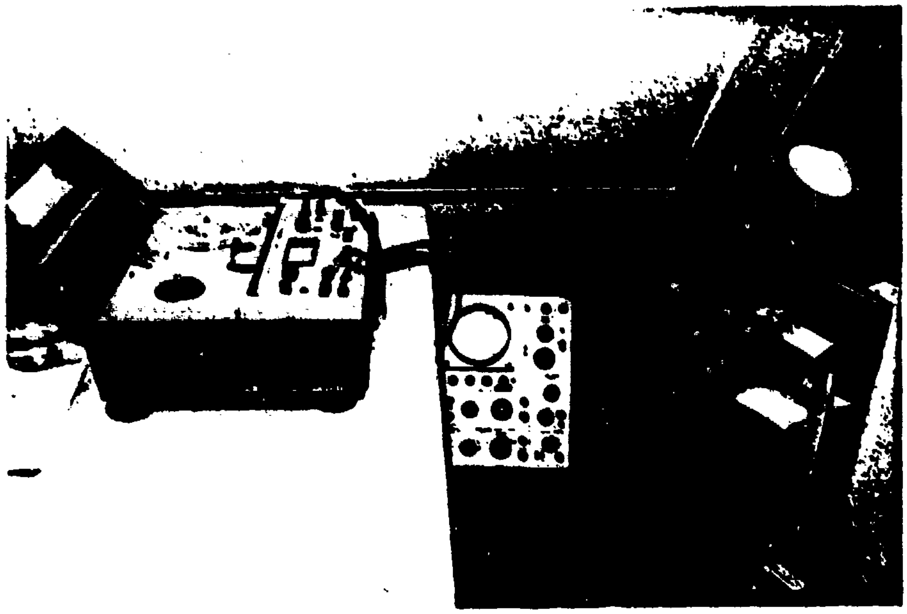

Figure 5. Beckman Dynograph Recorder and Hewlett-Packard FM Tape Recorder.

1 subject was 97 h; flight experience from the remaining 15 subjects ranged from 133 to 600 h with a mean time of 264 h. Simulator experience ranged from 20 to 70 h with a mean time of 41 h.

Experiment III. Twelve male general aviation pilots ranging in age from 20 to 33 years of age were used as subjects; the mean age was 23 years. The flight experience ranged from 100 to 1300 h with a mean flight time of 330 h. The average instrument flight time was 93 h with a range from 36 to 156 h. Simulator flight time ranged from 21 to 106 h with a mean time of 48 h. All subjects were nonsmokers and had fasted for 8 h prior to the start of each experimental session.

Experiment IV. Twelve male general aviation pilots ranging in age from 21 to 31 years of age were used as subjects; the mean age was 22 years. The flight experience ranged from 100 to 1730 h with a mean of 297 h. The average instrument flight time was 76 h with a range from 31 to 196 h. Simulator flight experience ranged from 21 to 86 h with a mean time of 40 h. All Subjects were nonsmokers and had fasted for 8 h prior to the start of each experimental session.

Procedures

Experimental Scenario

A basic experimental scenario used by ARL investigators to determine the effects of toxic compounds on pilot performance was used for the 4 experiments (8, 13, 14, 15, 21, 22). The scenario included a primary task, flying the simulator using standard instrument flight procedures, and a secondary task, the Sternberg Memory Search task. The primary task was representative of procedures that pilots typically perform when flying under IFR conditions. The secondary task was representative of communication tasks that increase

workload by requiring the pilot to receive, understand, and respond to verbal information.

Subjects in each of the 4 experiments participated in sessions that were approximatoly 4 h in duration. For Experiments I and II, the subjects completed a minimum of 2 training sessions. For Experiments III and IV, the subjects completed a minimum of 3 training sessions before the treatment sessions (referred to hereafter as "experimental sessions") started. The training sessions included practice with holding procedures, ILS approaches, and the Sternberg Memory Search task. Prior to the experimental sessions, each subject was tested for the ability to perform the primary task within the limits set by the Federal Aviation Administration Flight Test Guide for Instrument Pilot Candidates (25). The following limits were used: altitude deviation, +/- 30.48 m (100 ft); horizontal tracking deviation (localizer), +/- 1.5°; vertical tracking deviation (glide slope), +/- 0.7°; and rate of turn, less than 6°/s at any given time. Flight data were sampled once/second and the percent of samples outside the prescribed limits (% out) were determined. Performance during the training sessions for Experiments I and II was considered acceptable if the subject had less than 1% of the sample outside the prescribed limits for each performance variable. For Experiments III and IV, however, the performance criterion was 0% on all dependent variables. Several subjects received added training to bring their performance within tolerance limits.

A typical 4-h experimental session is depicted in Table 1. The experimental sessions were scheduled 1 week apart and included six 20-min simulator flights, each of which was followed by a 20-min rest period during which the simulator was not flown. During the rest periods, medical checks were performed as well as a variety of other activities which varied among the 4 experiments. Each experimental session started with a medical check. A registered nurse (RN) asked each subject his eating and sleeping habits over the previous 24 h and determined baseline pulse rate, blood pressure, and pupillary response. After the medical check, the subject flew one 20-min simulator flight to provide baseline data. During the next 20 min (the rest period), the subject was checked medically, physiological data were collected, and then the subject received the appropriate toxic substance. Five subsequent simulator flights were completed during which performance data on the primary and secondary tasks were collected. During the rest periods Breathalyzer readings were taken for Experiments I and IV. For Experiment IV the RN obtained a venous blood sample after flights 2 and 3. For Experiments III and IV, the subject performed the Sternberg Memory Search task as a single task during the final 4 rest periods. All data were collected under double-blind conditions.

Experimental Design

Experiment I. Four levels of ethyl alcohol were administered to each subject during the 4 experimental sessions. The amount of alcohol was adjusted for body weight and build (estimated body fat) to produce the following target percent BALs 0.0%, 0.225%, 0.045%, and 0.09% (26). The Latin Square within subjects, repeated measures design (Plan 12 described by Winer (27)) was used to balance BAL order effects for the MANOVA and the analysis of variance (ANOVA) procedures. This plan assumes that treatment, experimental session, and flight are fixed effects and subjects within the groups is a

TABLE 1. TYPICAL EXPERIMENTAL SESSION

Time	Activity
1300 - 1320	Medical check-in
1320 - 1340	1st simulator "flight" baseline data
1340 - 1400	Medical check, physiological baseline recording, symptoms questionnaire, and the administration of toxic substance
1400 - 1420	2nd simulator "flight"
1420 - 1440	Medical check, physiological recording, symptoms questionnaire, and single task (Sternberg) (if used)
1440 - 1500	3rd simulator "flight"
1500 - 1520	Medical check, physiological recording, symptoms questionnaire, and single task (Sternberg) (if used)
1520 - 1540	4th simulator "flight"
1540 - 1600	Medical check, physiological recording, symptoms questionnaire, and single task (Sternberg) (if used)
1600 - 1620	5th simulator "flight"
1620 - 1640	Medical check, physiological recording, symptoms questionnaire, and single task (Sternberg) (if used)
1640 - 1700	6th simulator "flight"
1700 - Release	Medical check, physiological recording, symptoms questionnaire, and medical surveillance
	TOTALS = 2 h in flight simulator
	4-h experimental session

random variable. Residual (1), the mean square (MS) for subjects (within groups) x treatment, was used as the error term to test for significance for (A) treatment, (B) experimental session, and (AB)' Latin Square error. Residual (2), the MS for subjects (within groups) x flight interaction, was used as the error term to test for the flight (C) main effect and flight x groups interaction. Residual (3) was used to test the AC and the BC interaction, and (AB)'C. The error terms were not pooled for any of the statistical analyses. Two subjects were randomly assigned to each group and each subject received each BAL condition. Five variables were tested for significance: (1) treat-

ment (BAL), (2) flight, (3) experimental session (column), (4) group (row), and (5) subject (nested within group). Also, 3 interactions were tested for significance: (1) treatment (BAL) x flight, (2) experimental session (column) x flight, and (3) group (row) x flight.

The subjects reported to the experimental session in a fasting state. Prior to the first flight, the subjects received one piece of toast. The first flight, for each experimental session, served as a baseline flight. Alcohol was administered during the rest period following the first flight. The drink consisted of 120 ml of distilled water and alcohol in appropriate proportions mixed with 306 ml of orange juice. The placebo had 4 ml of alcohol floated on top of the distilled water and orange juice mixture. Performance data on the primary and secondary tasks were collected during the 5 remaining flights, and BAL was measured during the 5 remaining rest periods.

Experiment II. The following commonly prescribed dosages for 3 drugs (promethazine hydrochloride: 25 mg; thiethylperazine: 10 mg; and cimetidine: 300 mg), standardized for a 70 kg person, and a placebo were administered to each of the 16 subjects over the course of 4 experimental sessions during Experiment II. A 4 x 4 Latin Square within subjects, repeated measures design, described earlier for Experiment I, was used to balance drug order effects for the MANOVA and ANOVA procedures. Four subjects were randomly assigned to each cell and each subject received each of the 3 drugs and placebo. Five variables were tested for significance: (1) treatment (drug), (2) flight, (3) experimental session (column), (4) group (row), and (5) subject (nested within group). Three interactions were tested for significance: (1) treatment (drug) x flight, (2) experimental session (column) x flight, and (3) group (row) x flight.

The height and weight tables of Freireich et al. (28) were used to determine the quantity of drugs to be administered to each subject. The body surface area was used to determine drug quantity (mg/m^2) to equate dosages to those used by Mattsson et al. (1). The 3 drugs and placebo control were administered in opaque capsules. The placebo capsules contained lactose, and the drug capsules contained the appropriate drug quantity and lactose to achieve an identically weighted capsule for each subject for the 4 experimental sessions.

The fasting subjects reported to the experimental session and underwent an initial medical interview conducted by an RN. The RN questioned each subject concerning his drug, food and liquid intake, and the amount of sleep he had had within the past 24 h. Then, the RN took the subject's pulse and blood pressure.

The first flight for each experimental session served as a baseline flight. The appropriate capsule was administered during the rest period following the first flight. Performance data on the primary and secondary tasks were collected for the remaining 5 flights. Respiration rate and ECG were recorded during the rest periods following the first, third, and fifth flights.

Experiment III. Three drug treatment conditions, a placebo (lactose) and 2 antiemetic drug combinations, were used for Experiment III. The following antiemetic drug combinations were used: (1) the thiethylperazine (10 mg) and

cimetidine (300 mg) combination (TC); and (2) the promethazine hydrochloride (25 mg), thiethylperazine (10 mg), and cimetidine (300 mg) combination (PTC). These drug quantities are for a 70 kg subject. For subjects who weighed more or less than 70 kg, the drug quantities were adjusted based on subject weight. The placebo and the 2 antiemetic drug combinations were administered to each of the 12 subjects over the course of 3 experimental sessions. A 3 x 3 Latin Square within subjects, repeated measures design, Winer plan 12 (27) described earlier for Experiment I, was used to balance drug order effects for the MANOVA and ANOVA procedures. Four subjects were randomly assigned to each cell and each subject received each of the 2 antiemetic drug combinations and the placebo. Five variables were tested for significance: (1) treatment (drug), (2) flight, (3) experimental session (column), (4) group (row), and (5) subject (nested within group). Three interactions were tested for significance: (1) treatment (drug) x flight, (2) experimental session x flight, and (3) group x flight.

The drugs and placebo were administered in opaque capsules. The placebo capsules contained lactose; the combination drug capsules contained the appropriate quantity of each drug and lactose to achieve an identically weighted capsule for each subject for the 3 experimental sessions.

<u>Experiment IV</u>. Three levels of ethyl alcohol were administered to each subject during the 3 experimental sessions: (1) a placebo which consisted of distilled water with 10 cc of 200 proof alcohol floated on top (0% BAL condition); (2) a medium dose calculated to yield 0.05% BAL; and (3) a high dose calculated to yield 0.10% BAL. One gram of 200 proof ethyl alcohol/kilogram body weight was used to produce a targeted BAL of 100 mg% (i.e., the high BAL condition (0.10% BAL)). For the medium BAL condition (0.05% BAL), 500 mg of 200 proof ethyl alcohol was mixed with distilled water to produce the following proportions: 1 part alcohol to 4 parts water. The total volume of the placebo, medium, and high doses was the same for a given subject. Alcohol treatments were administered after flight 1 and the subjects were given 15 min to consume the drink. The alcohol treatments were administered to each of the 12 subjects over the course of 3 experimental sessions during Experiment IV. A 3 x 3 Latin Square within subjects, repeated measures design, Winer Plan 12 (27) described earlier for Experiment I, was used to balance BAL order effects for the MANOVA and ANOVA procedures. Four subjects were randomly assigned to each cell and each subject received each BAL. Five variables were tested for significance: (1) treatment (BAL), (2) flight, (3) experimental session (column), (4) group (row), and (5) subject (nested within group). Three interactions were tested for significance: (1) treatment (drug) x flight, (2) experimental session (column) x flight, and (3) group (row) x flight.

During all 4 experiments, the flight performance and Sternberg Memory Search task data were automatically recorded onto 8-in. magnetic diskettes for each experimental session. Following each flight or single task data collection period, the raw data files underwent preliminary analysis and were stored on diskettes for subsequent analysis.

The results of the experimental sessions were compiled into a master summary file and transferred to a mainframe computer for statistical analysis using the Statistical Analysis System (SAS) package (29). The SAS procedures used included: standardizing variables, ANOVA, and MANOVA. The SAS uses the general linear model procedure when the data set contains unequal cell sizes.

Primary Task

The primary task consisted of three procedures: (1) a direct entry to a holding pattern, (2) the execution of 3 holding patterns, and (3) a simulated ILS approach for landing (Fig. 6). These maneuvers were performed during a 20-min simulator flight. The task, flown in a no-wind condition with randomly generated vertical turbulence (± 300 ft/min), started 5 mi from the outer marker (OM) (point △ in Fig. 6) on a localizer magnetic bearing of 313° to runway 31, at an altitude of 914 m (3000 ft) with slow cruising power, landing gear up, and flaps one-third extended.

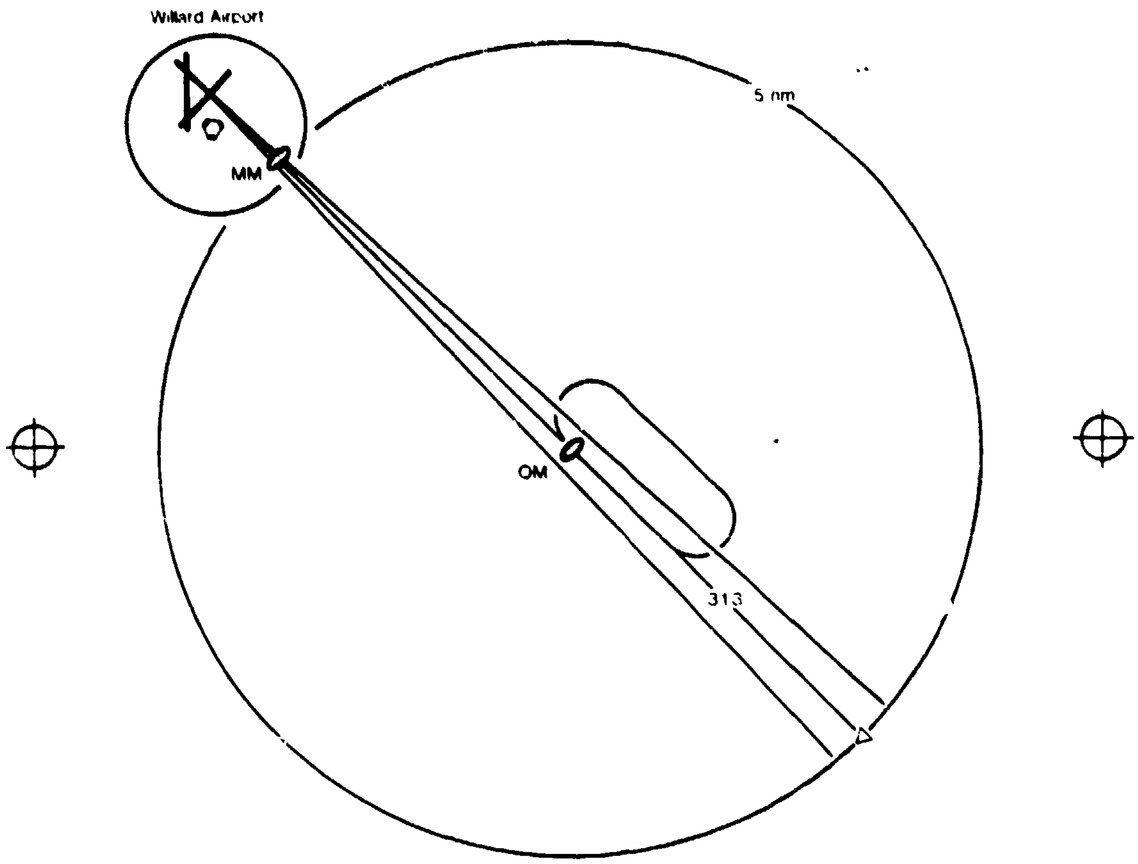

Figure 6. Primary task (holding pattern and ILS approach to Willard Airport).

The bearing of 313° represented the extended centerline of runway 31. The OM compass locator, a low-frequency nondirectional beacon (NDB), provided signals to the automatic direction finder (ADF) in the cockpit. A light on the simulator instrument panel was activated when the aircraft approached the outer marker (OM). When the aircraft was directly over the OM, the ADF indicator rotated 180°, which indicated passage over the NDB. The subject was instructed to track the localizer to the OM, execute three holding patterns,

and complete an ILS approach. The standard holding pattern was oval and the subject was required to execute a 180° standard rate turn (3° of turn/second), track an outbound heading of 133° for 1 min, complete a second 180° standard rate turn, and track inbound on the localizer for 1 min. The holding pattern was initiated and completed at the OM.

Prior to completion of the third holding pattern, the computer generated an audio clearance for the ILS approach. The ILS approach from the OM to the runway consisted of a two-dimensional tracking task involving indicators that operate independently. The subjects used a standard ILS approach instrument (the top, center instrument) for this task (Fig. 7). The vertical indicator, the localizer of the ILS instrument, represented the extended runway centerline bearing of 313° and provided lateral tracking information. The deflection limits of the localizer indicator were +/- 1.5°. The horizontal indicator, the glide slope of the ILS instrument, represented a 3° angle of descent to the runway and provided vertical tracking information. The deflection limits of the glide slope indicator were +/- 0.7°. The difficulty of the tracking task increased as the runway was approached. The subject was instructed to keep both tracking needles centered. The glide slope trajectory is illustrated in Figure 8. The approach terminated with a simulated landing on runway 31.

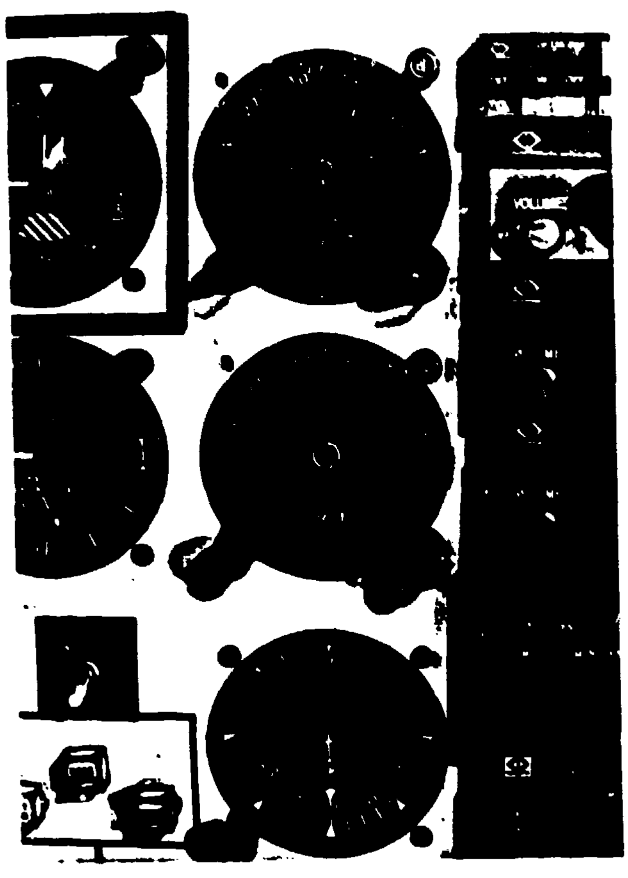

Figure 7. ILS indicator.

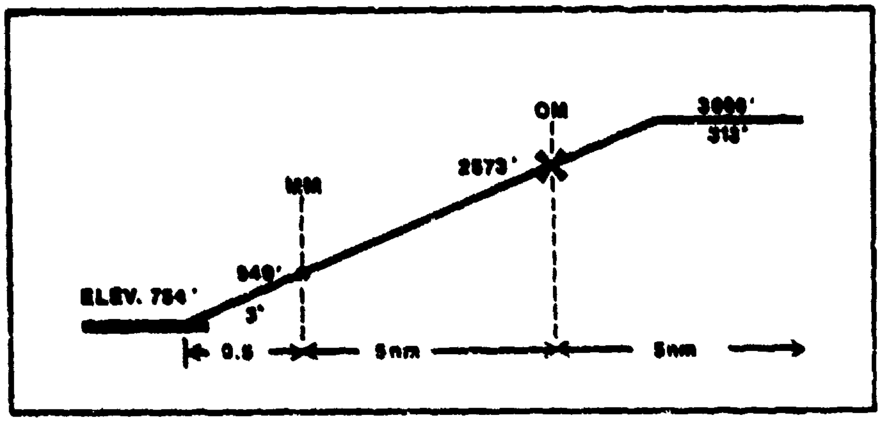

Figure 8. Glide slope trajectory.

The primary flight variables for Experiments I and II were: altitude straight and level (ALT 1), altitude while turning (ALT 2), LOC tracking, and GLS tracking. For Experiments III and IV, these 4 dependent variables and rate of turn straight and level (TC 1), and rate of turn while turning (TC 2) were used. The flight parameters, altitude and rate of turn, were sampled at the rate of 1 Hz during the hold phase, while LOC and GLS were sampled during the approach phase. The primary task variables (Table 2) were separated into 10 s arrays that contain the secondary task and those that do not.

TABLE 2. PRIMARY TASK DEPENDENT VARIABLES

Variable	Flight Phase	Definition
ALT 1	Hold	Altitude error (while straight and level)
ALT 2	Hold	Altitude error (while turning)
TC 1	Hold	Turning rate control (while straight and level)
TC 2	Hold	Turning rate control (while turning)
LOC	Approach	Localizer (lateral) tracking error
GLS	Approach	Glide slope (vertical) tracking error

Secondary Task

During the flight, the Sternberg Memory Search task was randomly presented as a secondary task to increase the workload of the subject. The secondary task consisted of the presentation of a warning signal, followed by an MSET of 3 letters (1-s later) for Experiments I and II and an MSET of either 2 or 4 letters for Experiments III and IV. The positive set was randomly generated for each presentation from a pool of 18 letters. For Experiments III and IV, presentation of the MSET of 2 or 4 letters was alternated. The letters were presented by a voice synthesizer. The test probe letter, which had a 50% probability of being a member of the MSET, was presented 2 s after the last letter of the set for Experiments I and II and 4 s after the last MSET letter, for Experiments III and IV.

The subject was instructed to press the thumbswitch forward on the control wheel if the probe was a member of the positive set (true), and to pull backward if the test letter was not a member (false) (30). The subject was instructed to move his left thumb to the switch upon hearing the warning tone. Reaction time was recorded with a resolution of 33 ms, and if a response was not given within 4 s, then an error was recorded. The presentation of the secondary task required 10 s; the secondary task was programmed to occur randomly at a 40% probability (i.e., 48 times out of 120 possible 10-s intervals during a 20-min flight) for Experiments I and II and at a 50% probability (i.e., 60 times out of 120 possible 10-s intervals during a 20-min flight) for Experiments III and IV.

Prior to each experimental session, the subjects were instructed to "Aviate first; navigate second; and communicate last," which was intended to establish the following priorities: first, control the aircraft; second, practice appropriate instrument procedures; and third, respond to the Sternberg Memory Search task.

RESULTS

Experiment I

The results of Experiment I, which evaluated the effects of 4 BALs on pilot performance to determine the sensitivity of a pilot performance measurement methodology, was reported by Taylor et al. (8) and are repeated here.

The results of using the Breathalyzer to determine BAL indicated that all subjects, with the possible exception of one subject in the 0.0225 BAL experimental condition and one in the 0.045 BAL condition, were administered the programmed amount of alcohol. The highest BAL readings for these two subjects for the stated conditions were 0.000 and 0.008, respectively. An error in preparing the alcohol drink was suspected. Excluding these two errors, there was no overlap on the distribution of scores. The 0.000 BAL condition had only two values greater than zero: 0.003 and 0.004. The 0.0225 BAL experimental condition had a measured median value of 0.014 and a range of 0.011-0.017; the 0.045 BAL condition had a measured median value of 0.038 and a range of 0.031-0.041; the 0.090 condition had a measured median value of 0.082 and a range of 0.072-0.093. For all BALs except for the 0.0

BAL condition, the median measured BAL was less than the target BAL. All further reference to BAL refers to target BAL.

Lateral ink tracings of the tracking task were recorded for all flights and analyzed to determine if the subjects were able to successfully complete the primary task. Visual examination of the tracings of the holding patterns and the ILS approach for all experimental conditions indicated that each subject was able to complete the procedures and fly the simulator to the middle marker (MM). The MM is the point at which the pilot takes over visually to land the aircraft on an ILS approach. All subjects completed every flight with the exception of one subject in the highest BAL condition who experienced severe nausea and was unable to complete one flight. For all subjects except one, however, visual inspection of the tracings comparing the 0.09 BAL condition with the 0.0 BAL condition indicated the effects of alcohol on pilot performance. Performance on the primary task typical for the BAL 0.0 experimental condition resulted in holding patterns that were essentially superimposed, and there was no evidence of significant deviation from the extended centerline. The performance typical for the BAL 0.0 condition is shown in Figure 9.

The performance typical for the BAL 0.09 experimental condition is shown in Figure 10. Effects include erratic lateral tracking and extended inbound and outbound legs on the holding patterns. Deviation outside the lateral tracking limit was also observed just prior to the MM.

Flight data for heading, airspeed, relative bearing, rate of turn, and lateral and vertical tracking were sampled once/second; and 4 RMS deviation values were computed. The RMS deviations were computed for altitude straight and level (ALT 1), and altitude while turning (ALT 2) for the entry into the holding pattern and 3 holding patterns. Root mean square deviations were computed for LOC during the entire flight, and for GLS during the ILS approach. The mean RMS values for the 4 dependent variables (ALT 1, ALT 2, LOC, and GLS) were computed for each of the 4 BALs. The means and standard error of the means for the 4 BALs for all subjects during the last 5 flights (post alcohol) for each dependent variable are shown in Figures 11 through 14. The means for all 4 variables showed a monotonic increase from 0.0 through 0.09 BAL.

Data for 4 dependent variables for the primary task (the RMS deviations of the 2 altitudes, and RMS deviations of the lateral and vertical tracking) were transformed using a log transformation. The transformed scores for all 8 subjects during the last 5 flights (post alcohol) were used in a MANOVA to test the main effects of treatment (BAL), flight, experimental session (column), group (row), and subject (nested within group). The data set contained 156 observations out of 160 possible observations; 4 observations were lost. One subject experienced nausea and was unable to complete one flight; the remaining 3 unavailable observations resulted from computer malfunctions. An approximate F-test, based on Wilks' criterion (31), resulted in $F(12,24) = 1.64$ ($P<0.1469$) for the treatment main effect (BAL level). An approximate F-test was conducted using as the error term the interaction, flight x subject (nested within group), to test the significance of the flight main effect. The test resulted in an $F(16,40) = 2.49$ ($P<0.0099$). The treatment (BAL level) was not significant, but the flight main effect was significant. The main effect of subject (nested within group) was significant,

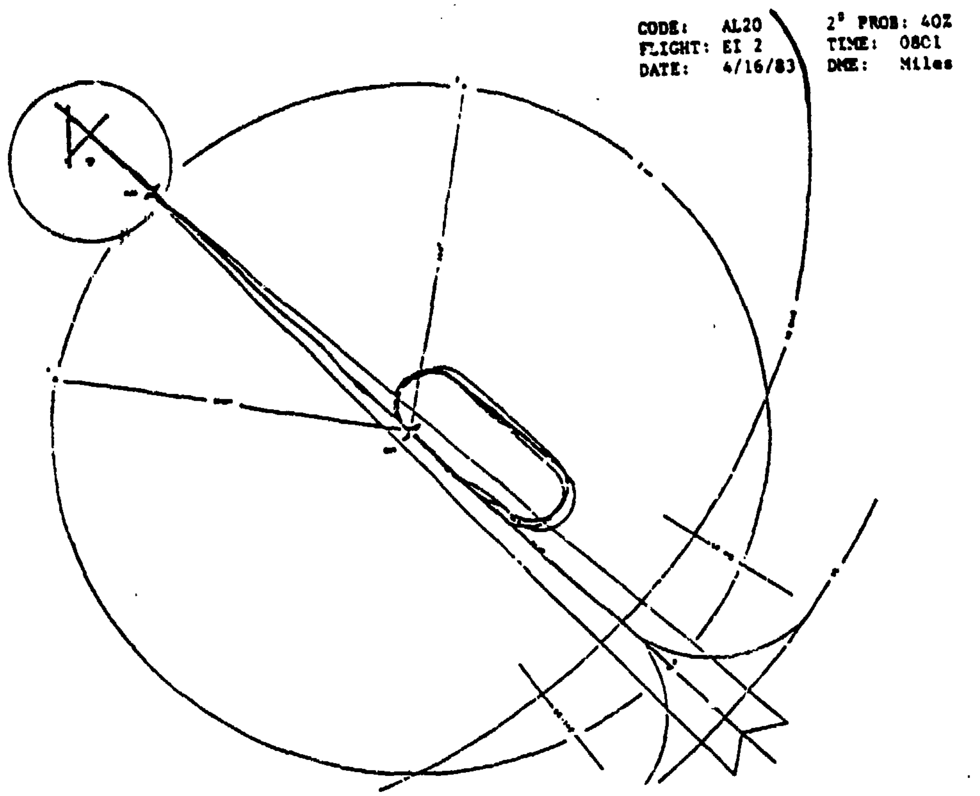

Figure 9. Lateral tracking (LOC), subject AL20, BAL 0.0, flight 2.

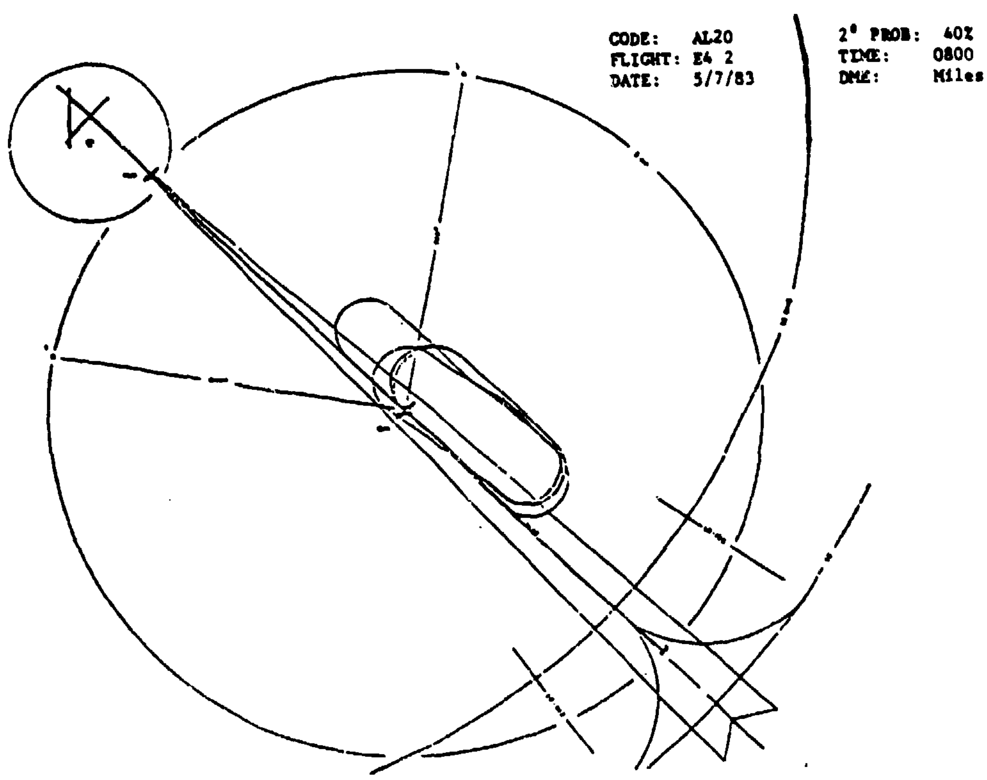

Figure 10. Lateral tracking (LOC), subject AL20, BAL 0.09, flight 2.

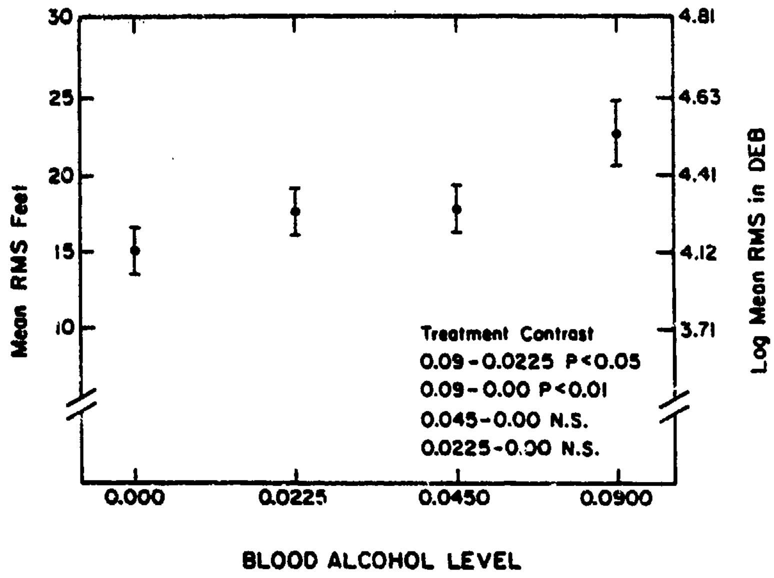

Figure 11. RMS means and standard error of the means by each BAL for ALT 1 variable (5 post-alcohol ingestion flights, 8 subjects), N = 40.

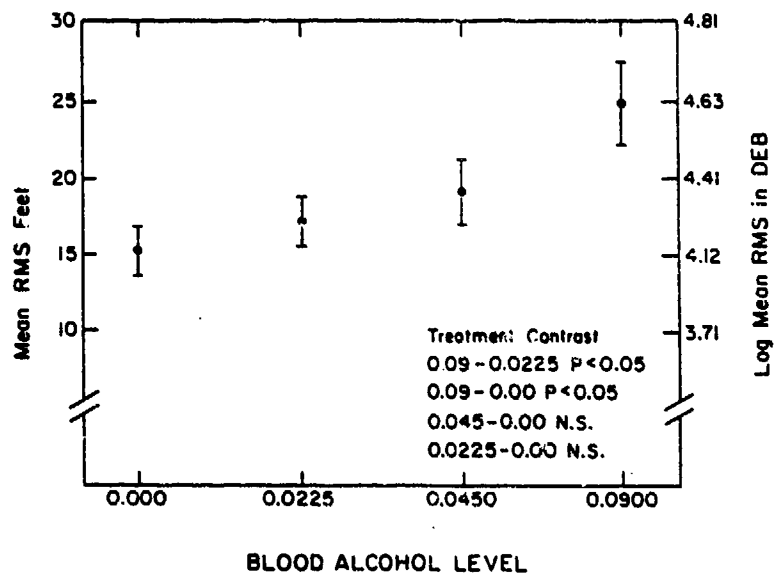

Figure 12. RMS means and standard error of the means by each BAL for ALT 2 variable (5 post-alcohol ingestion flights, 8 subjects), N = 40.

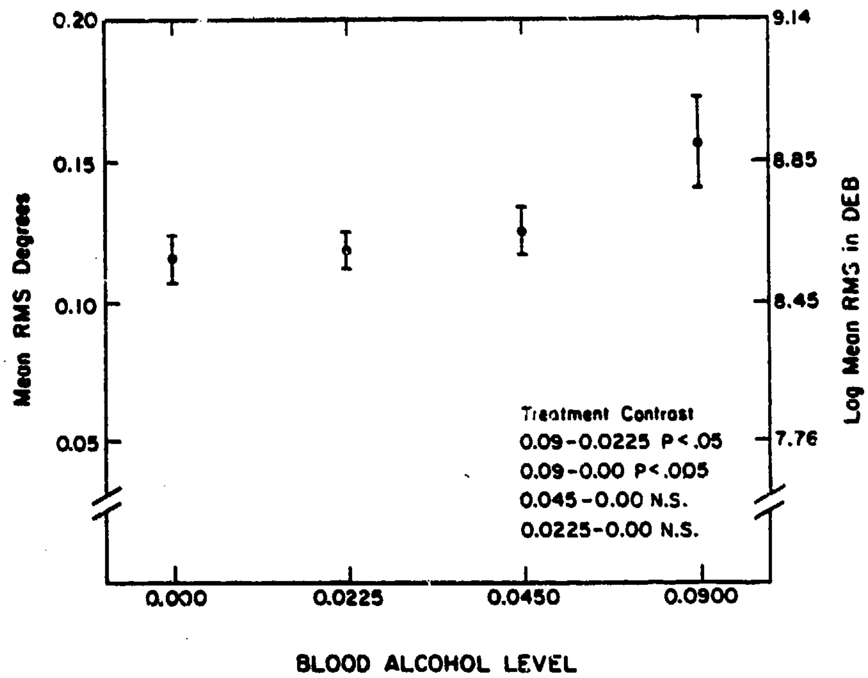

Figure 13. RMS means and standard error of the means by each BAL for GLS variable (5 post-alcohol ingestion flights, 8 subjects), N = 40.

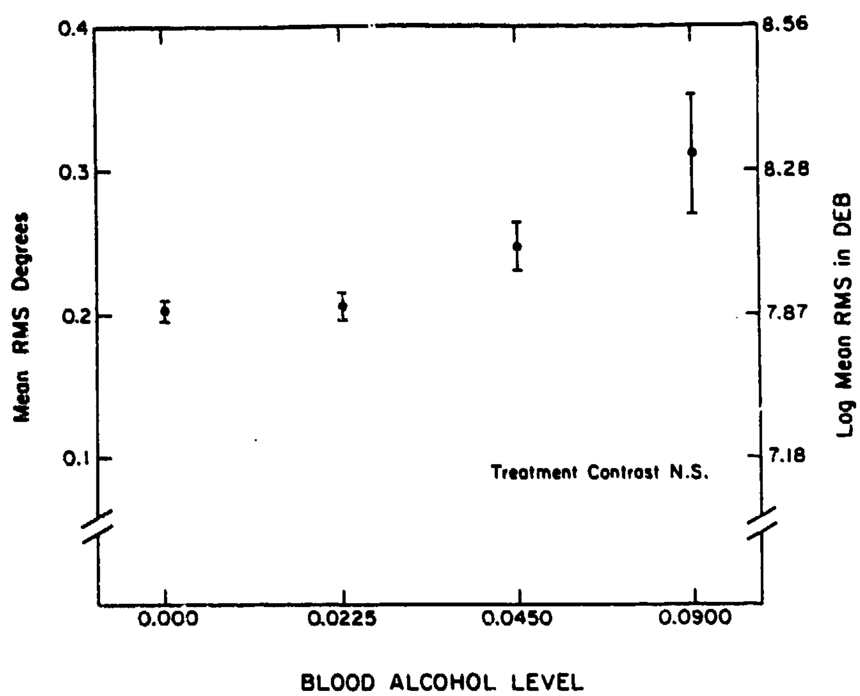

Figure 14. RMS means and standard error of the means by each BAL for LOC variable (5 post-alcohol ingestion flights, 8 subjects), N = 40.

F(16,199) = 14.05 (P<0.0001). The main effects of experimental session (column) and group (row) were not significant.

Univariate ANOVA were computed for each primary task dependent variable using all subjects (24); a summary of the analysis is presented in Appendix A. The analyses of 3 of the 4 variables (ALT 1, ALT 2, and GLS) resulted in a significant treatment (BAL) main effect. The LOC variable was not significant. Contrasts were computed between the 0.0 BAL and the other 3 BAL conditions and between the 0.0225 BAL and the 0.09 BAL. Table 3 summarizes the results of the contrasts. None of the contrasts between BAL 0.0 and 0.0225 and between 0.0 and 0.045 were significant, but 3 of the contrasts between 0.0 and 0.09 and between 0.0225 and 0.09 were significant.

The univariate analyses for the altitude control while turning (ALT 2) and vertical tracking (GLS) variables resulted in significant main effects for flight: ALT 2, $F(4,16) = 3.93$ ($P<0.02$); GLS, $F(4,16) = 3.11$ ($P<0.05$).

The computer random number generator malfunctioned during Experiment I. The random number generator was used to determine the sequence in which the three-letter sets of the secondary task were presented. The malfunction resulted in a repetitive pattern of sets of stimuli being presented. Since some experimental sessions were conducted with random sets of secondary task stimuli and some sessions with repetitive sets being presented, the reaction time data were discarded. The incorrect responses for the secondary task were also discarded.

TABLE 3. SIGNIFICANCE PROBABILITIES OF CONTRASTS BETWEEN BALs FOR THE DEPENDENT VARIABLES

Dependent variables	BAL conditions			
	0.0 - 0.0225	0.0 - 0.045	0.0 - 0.09	0.0225 - 0.09
ALT 1	NS	NS	0.0091	0.0473
ALT 2	NS	NS	0.0029	0.0149
GLS	NS	NS	0.0049	0.0121
LOC	NS	NS	NS	NS

NS = Not Significant

Experiment II

The results of Experiment II, which evaluated the effects on pilot performance of the commonly prescribed dosages of promethazine hydrochloride (25 mg), thiethyperazine (10 mg), and cimetidine (300 mg) taken singly, were reported by Taylor et al. (8) and are repeated here.

The lateral ink tracings that were recorded for the flight task for the holding pattern and localizer portion of the ILS were analyzed to determine if the subjects were able to successfully complete the primary task. Visual examination of the holding patterns and the ILS approach for all experimental conditions for each subject indicated that each subject completed the primary task for each flight (i.e., flew the simulator to the MM). Comparisons of the flights for each of the 3 antiemetic drugs with the control flights indicated no consistent patterns of gross differences. The performances that were typical for the control (placebo) and the promethazine hydrochloride conditions are shown in Figures 15 and 16.

The flight data sampling and the RMS computations described for Experiment I were also performed for Experiment II. The mean RMS values for the 4 dependent variables (ALT 1, ALT 2, LOC, and GLS) were computed for each of the 4 experimental treatment conditions (drug). The means and the standard error of the means for the treatment conditions for all subjects during the last 5 flights (post drug) are shown in Figures 17 through 20. For all 4 dependent variables, the RMS mean for promethazine hydrochloride was higher than the control mean. Examination of the means for the RMS LOC dependent variable indicated that the RMS means for thiethylperazine and cimetidine were lower than the control mean.

The scores for the 4 dependent variables for the primary task, the RMS deviations of the 2 altitudes (ALT 1 and ALT 2), and the RMS deviations of the lateral and vertical tracking (GLS and LOC) were transformed using a log transformation. The transformed scores for all 16 subjects during the last 5 flights (post drug) were used in a MANOVA to test the main effects of treatment (drug), flight, experimental session (column), group (row), and subject (nested within group). The data set contained 314 observations out of 320 possible observations; 6 observations were lost due to computer malfunctions. An approximate F-test, based on Wilks' criterion, resulted in $F(12,87) = 2.47$ ($P<0.008$) for the treatment main effect (drug). The MANOVA tests of significance for the main effects for flight and group, and for the interactions for experimental session (column) x flight, treatment (drug) x flight, and flight x group (row) were not significant. The main effect of subject (nested within group) resulted in an $F(48,614) = 21.80$ ($P<0.0001$). An approximate F-test of the main effect of experimental session (column) based on Wilks' criterion resulted in $F(12,87) = 2.64$ ($P<0.0046$). The RMS means and standard error of the means across 16 subjects for all treatment conditions for the localizer for the 4 experimental sessions are shown in Figure 21. The means show a monotonic decrease across the 4 sessions. The performance increase on the LOC tracking variable indicated that the subjects were not stabilized when experimental session 1 began.

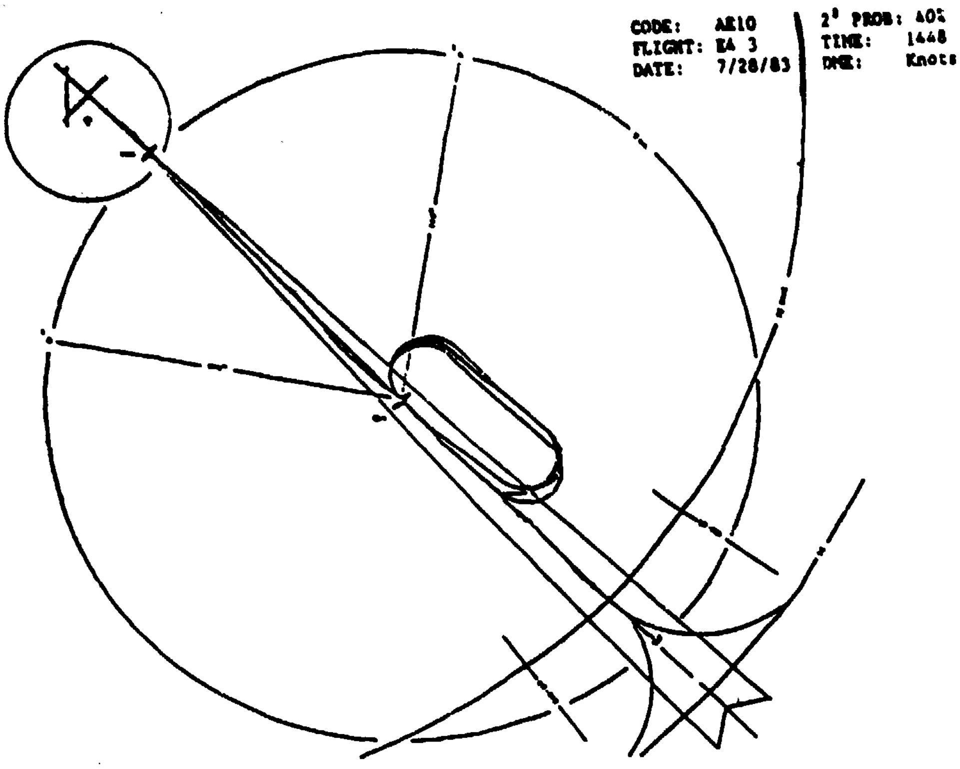

Figure 15. Lateral tracking (LOC), subject AE10, placebo, flight 3.

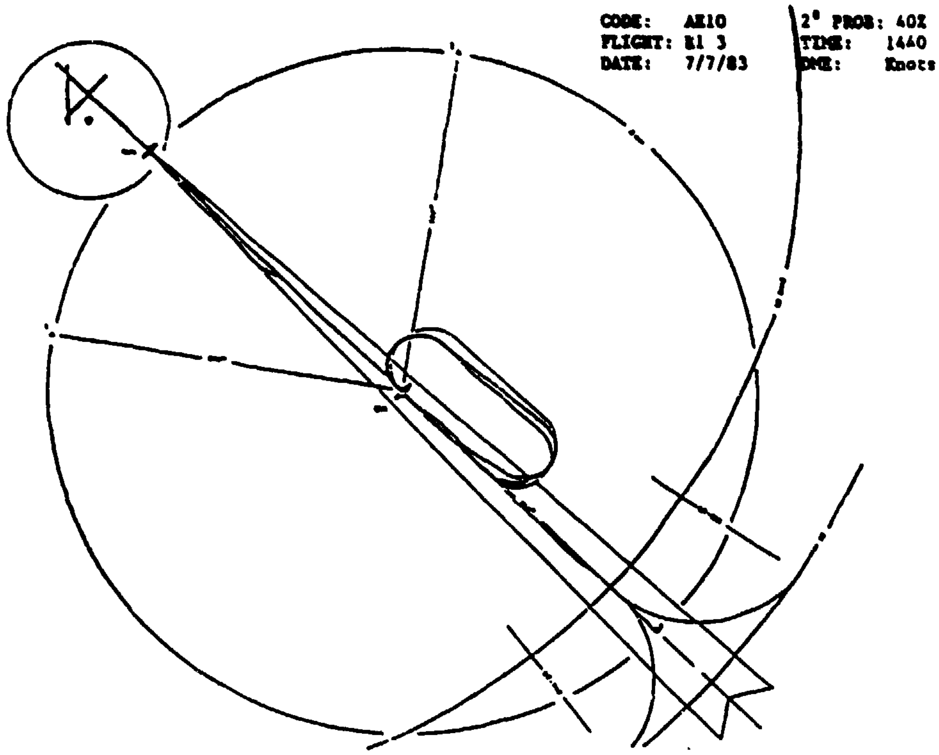

Figure 16. Lateral tracking (LOC), subject AE10, promethazine hydrochloride, flight 3.

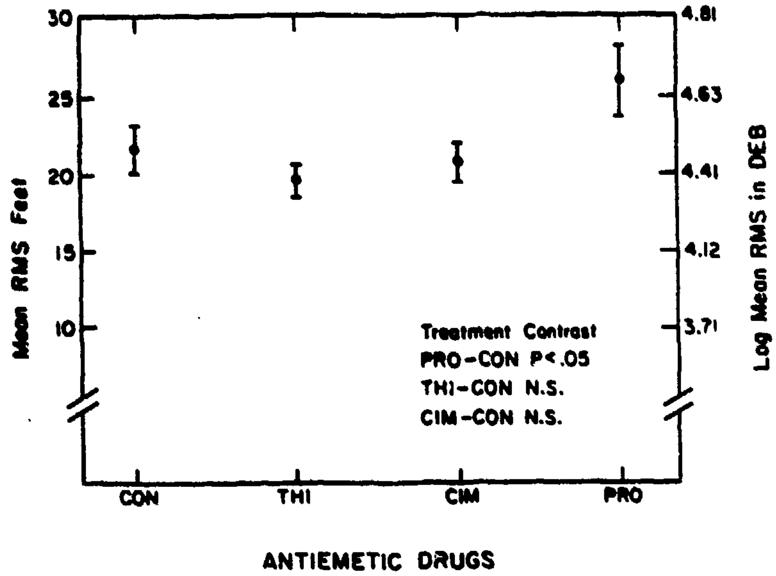

Figure 17. RMS means and standard error of the means by each antiemetic drug condition for ALT 1 variable (5 post-drug flights, 16 subjects), N = 80.

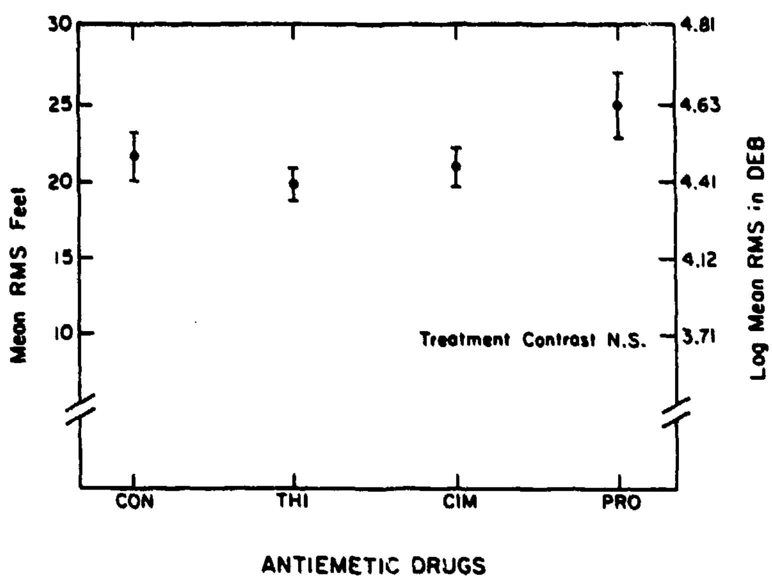

Figure 18. RMS means and standard error of the means by each antiemetic drug condition for ALT 2 variable (5 post-drug flights, 16 subjects), N = 80.

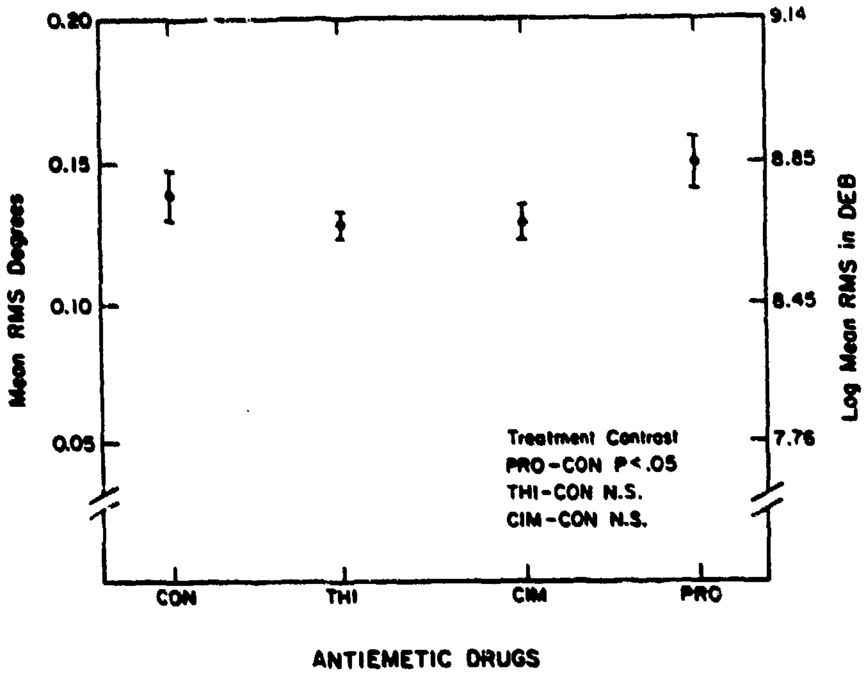

Figure 19. RMS means and standard error of the means by each antiemetic drug condition for GLS variable (5 post-drug flights, 16 subjects), N = 80.

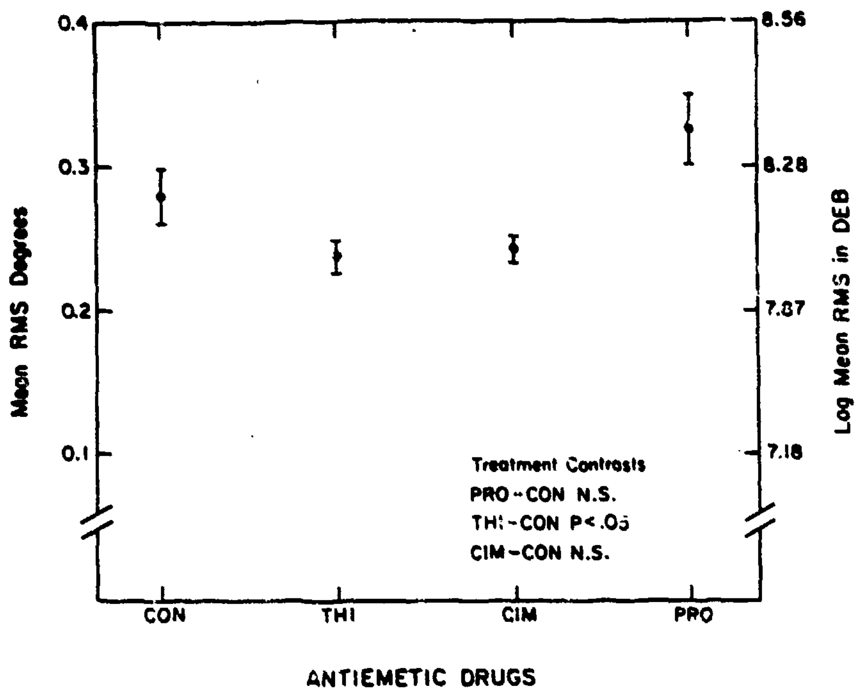

Figure 20. RMS means and standard error of the means by each antiemetic drug condition for LOC variable (5 post-drug flights, 16 subjects), N = 80.

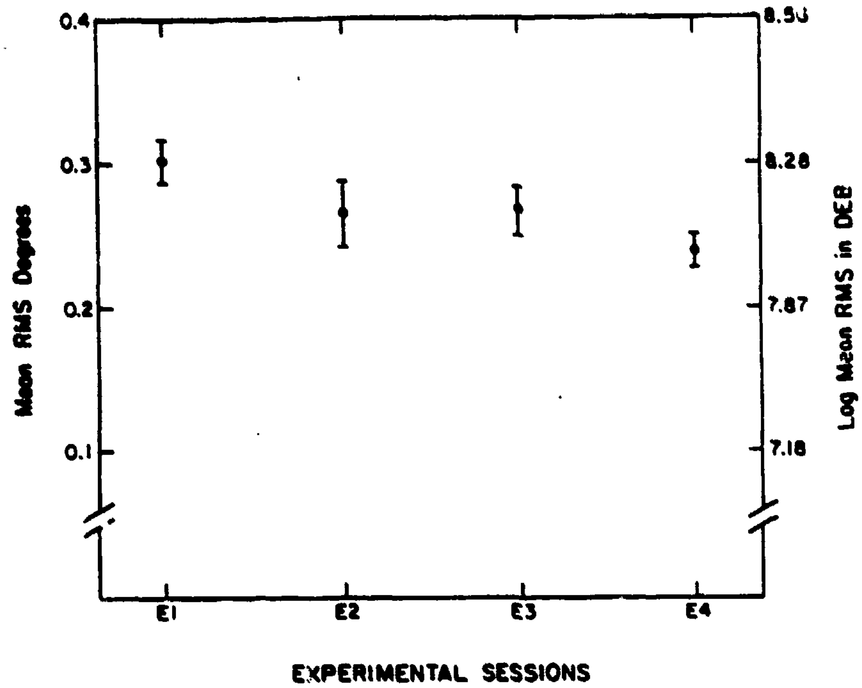

Figure 21. RMS means and standard error of the means by experimental session for LOC variable (16 subjects), N = 16.

Univariate analyses were computed for each primary task dependent variable using all subjects; a summary of the analyses is presented in Appendix B. The analyses of 2 of the variables (ALT 1 and LOC) supported the findings of the MANOVA test of a significant treatment (drug) main effect. The treatment main effect for ALT 2 and GLS was not significant. The F-tests produced the following results: ALT 1, $F(3,36) = 4.12$ $(P<0.0131)$; and LOC, $F(3,36) = 8.12$ $(P<0.003)$. Contrasts for the univariate analysis for the treatment (drug) effect between the control and each of the antiemetic drugs were determined using the MS for drug x subject (groups) as the error term. The results of the contrasts are summarized in Table 4.

A significant difference was found between the control and promethazine hydrochloride for ALT 1 and GLS, but not between the control and either cimetidine or thiethylperazine for these dependent variables. The contrasts for ALT 2 were not significant. For the LOC dependent variable, contrasts between the control and thiethylperazine were significant. A review of Figure 20 indicates that the RMS mean for thiethylperazine was lower than the control mean.

Univariate analyses for the 4 dependent variables for the experimental session main effect resulted in a significant F-test for the LOC variable, $F(3,36) = 7.86$ $(P<0.0004)$. The other 3 dependent variables were not significant.

TABLE 4. SIGNIFICANCE PROBABILITIES OF CONTRASTS BETWEEN THE CONTROL AND EACH ANTIEMETIC DRUG FOR THE DEPENDENT VARIABLES

Dependent variables	Treatment contrasts		
	CON-CIM	CON-THI	CON-PRO
ALT 1	NS	NS	0.0184
ALT 2	NS	NS	NS
GLS	NS	NS	0.0291
LOC	NS	0.013	NS

NS = Not significant

During Experiment II, the random number generator for the Sternberg Memory Search task malfunctioned for 4 of the antiemetic subjects. The hit (true) and the correct rejection (false) reaction times were discarded for these subjects. The data pertaining to the incorrect responses for the secondary tasks were also discarded for these 4 subjects.

For the remaining 12 subjects, the true and the false reaction times were used in a MANOVA to test the main effects of treatment (drug), flight, experimental session (column), group, and subject (nested within group). An approximate F-test, based on Wilks' criterion, resulted in $F(6,70) = 3.35$ $(P<0.0059)$ for the treatment (drug) main effect. The main effects of experimental session, flight, and group were not significant, but subject (nested within group) resulted in an $F(24,322) = 16.81$ $(P<0.0001)$.

Univariate analyses for the true reaction times and the false reaction times were computed. No significant main effects were found for the true reaction time, but the analysis for the false reaction time resulted in $F(3,36) = 2.81$ $(P<0.05)$. Linear contrasts indicated that the effect was due to the differences between promethazine hydrochloride and cimetidine.

A stepwise logistic regression analysis was computed to determine the effect of the antiemetic drugs on accuracy for the secondary task. The analysis indicated that accuracy showed little variation as a result of the antiemetic drugs.

The ECG data collected during the 2 post-drug periods were digitized, and the MHP and the HPV were computed. The digitized data were analyzed to compute the variance of the heart period data for the frequency band associated with spontaneous respiration (i.e., 0.12 to 0.40 Hz). This variance, $\hat{V}$, and the HPV were transformed using a log transformation to normalize the distributions.

The MHP, the means for the HPV and the $\hat{V}$ distributions were computed. The MHP for the baseline condition (predrug following the first flight) and the 2 post-drug periods were examined. The means for the placebo and for the 3 antiemetic drugs showed a monotonic increase in heart period for the 3 post-flight data periods. From the baseline condition, the total heart period increase during the 2 post-drug periods was 100 ms for cimetidine, 110 ms for thiethylperazine, and 121 ms for both the placebo and promethazine hydrochloride. A univariate ANOVA was computed for MHP for the 2 post-drug rest periods (flights #3 and #5) to test the main effects of treatment (drug), flight, experimental session (column), group (row), and subject (nested within group). The drug effect results, $F(3,80) = 2.51$ ($P=0.063$), were not significant at the 0.05 level of confidence. The flight main effect was significant, $F(1,80) = 7.94$ ($P<0.05$). The experimental session and group main effects were not significant. The main effect of subject (nested within group) was significant, $F(12,80) = 37.77$ ($P<0.001$). The ANOVAs for the HPV and $\hat{V}$ were also computed using the same model described for the MHP analysis. The treatment main effect (drug) was not significant at the 5% alpha level for either of the two dependent variables.

Experiment III

The investigation of new drugs (IND) submission to the Federal Drug Administration (FDA) proposed a pilot study to investigate the gross toxicity effects of the TC and the PTC antiemetic drug combinations. The protocol called for administering 3 drug combinations to 3 volunteers on 3 separate days, and for measuring blood pressure, pulse, and subjective responses at 30-min intervals. The antiemetic drug combinations were as follows: TC (10 mg and 300 mg, respectively); PC (25 mg and 300 mg, respectively); and PTC (25 mg, 10 mg, and 300 mg, respectively). The University of Illinois Institutional Review Board approved the project with the stipulation that an additional procedure be added to the pilot study in which the 3 subjects be given one-half or less of the proposed maximum dose of a combination of thiethylperazine and promethazine hydrochloride. The following additional drug administration was added to the pilot study protocol: thiethylperazine, 5 mg and promethazine hydrochloride, 12.5 mg. The results of the pilot study indicated no remarkable side effects such as sedation nor any remarkable elevation in blood pressure or pulse rate.

A summary of the side effects for each of the combination antiemetic drug treatments administered in Experiment III is presented in Table 5. The symptoms were taken from the nurse checklist and questionnaire, and from the subject symptom checklist which was completed after each of the 6 experimental flights comprising a single experimental session. According to the experimental protocol, the subjects' vital signs were also checked following each experimental flight.

Sleepiness and fatigue were the most prevalent symptoms (Table 5); there were no serious medical symptoms. The bradycardia that subject AC01 experienced while taking the combination of the antiemetic drugs was not reflexive to blood pressure changes, and it lasted approximately 1 h. The subject was not aware of any changes and failed to report these changes. The bradycardia was observed during the monitoring of vital signs. Also, for the PTC drug combination, subject AC03 experienced elevated blood pressure and

TABLE 5. SUMMARY OF SIDE EFFECTS FOR COMBINATION ANTIEMETIC DRUGS

Subject	Placebo	TC	PTC
AC01	None	None	Bradycardia: Mid 40s as compared to Mid 60s
AC02	None	None	Sleepy and fatigued
AC03	None	Fluttery chest, racing heart, vitals are normal	Elevated BP and HR
AC04	Sleepy--4 h sleep night before	Sleepy--4 h sleep night before	None
AC06	None	None	Sleepy and fatigued
AC07	Slight sleepiness	Slight sleepiness	Slight sleepiness
AC08	None	None	Sleepy and fatigued
AC09	Very sleepy and fatigued	Slight sleepiness and fatigue	Very sleepy and fatigued
AC10	None	None	None
AC11	None	None	Extreme sleepiness and fatigue--3 h sleep night before
AC13	None	None	Sleepy
AC14	None	None	Sleepy and fatigued

heart rate (142/84 and 90, respectively) as compared to the control condition (120/75 and 70, respectively). These readings appeared prior to drug administration and remained throughout the session, so we assumed that it was unrelated to the PTC combination. The nurse questionnaire indicated that the subject had only 3 h sleep during the previous evening. The same subject indicated a subjective experience of racing heart and fluttery chest during the TC combination drug experimental session, but the vital signs were normal.

Subject AC05 represents a special case. This individual complained of sleepiness and fatigue during all 3 experimental sessions (placebo, TC combination, and PTC combination). The subject also showed performance decrements during the placebo condition and was generally considered an uncooperative subject by the experimenter. Subject AC05's data was so poor, and he was so uncooperative, that he was eliminated from the project. He is not included in the table of symptoms.

To summarize, 3 out of 12 subjects showed symptoms that appeared to be related to sedation during the placebo condition. During the TC combination condition, the same 3 subjects circled sleepy and fatigued on their symptoms checklist. During the PTC combination condition, 8 out of 12 subjects circled the symptoms of fatigue and sleepiness. It appears, based on these findings, that the primary side effects that are commonly perceived are effects of sedation for the PTC condition.

The flight data from the primary task were used to compute RMS values for the 6 dependent variables for each of the 3 experimental treatment conditions (2 antiemetic drug combinations and the placebo) for each of the 12 subjects. The RMS scores for the 6 dependent variables for the primary task were transformed using a log transformation. The log RMS scores for the 12 subjects for the 5 post-drug flights were used in a MANOVA to test the main effects of treatment (drug), flight, experimental session (column), group (row), and subject (nested within group). The data set contained 179 of 180 possible observations; one observation was lost due to a computer malfunction. An F-test, based on Wilks' criterion resulted in $F(12,26) = 3.89$ $(P<0.0018)$ for the treatment (drug) main effect. An F-test of the flight main effect based on Wilks' criterion resulted in $F(24,109) = 3.14$ $(P<0.0001)$. The group and experimental session main effects were not significant. The treatment x flight interaction, $F(48,368) = 1.65$ $(P<0.0059)$, was the only significant interaction. An F-test of the subject (nested within group) main effect resulted in an $F(54,381) = 15.46$ $(P<0.0001)$.

Univariate analyses were computed for the 6 primary task dependent variables for the 12 subjects. A summary of the analyses is presented in Appendix C. The results of the analyses indicated that 3 of the dependent variables (TC 1, TC 2, and LOC) supported the findings of the MANOVA test of a significant treatment (drug) main effect, but the treatment main effects for ALT 1, ALT 2, and GLS were not significant. The significant ANOVAs using MS for drug x subject (nested within group) as an error term are as follows: TC 1, $F(2,18) = 7.42$ $(P<0.0045)$; TC 2, $F(2,18) = 5.65$ $(P<0.0124)$; LOC, $F(2,18) = 18.33$ $(P<0.0001)$. Contrasts between the treatment conditions for the 3 significant dependent variables were examined by Tukey's Studentized Range Tests. A summary of these tests is presented in Table 6.

TABLE 6. TUKEY'S STUDENTIZED RANGE TESTS BETWEEN THE 3 DRUG CONDITIONS FOR THE 3 SIGNIFICANT DEPENDENT VARIABLES

Dependent variables	Treatment contrast		
	PCB-TC	PCB-PTC	TC-PTC
TC1	NS	*	*
TC2	NS	NS	*
LOC	NS	*	*

*$p < 0.05$
NS = Not Significant

PCB = Placebo
TC = Thiethylperazine and Cimetidine Combination
PTC = Promethazine hydrochloride, Thiethylperazine, and Cimetidine Combination

The contrasts between the placebo and the thiethylperazine-cimetidine (TC) combination were not significant. All of the contrasts between the TC and the promethazine hydrochloride, thiethylperazine, and cimetidine (PTC) combination were significant. Two of the three variables (TC 1 and LOC) had significant contrasts between the placebo and the PTC combination.

The RMS means and the standard error of the RMS means for the 3 treatment conditions for the 12 subjects, averaged over the 5 post-drug flights, are shown in Figures 22 through 27 for each of the 6 dependent variables (ALT 1, ALT 2, TC 1, TC 2, LOC, and GLS, respectively). Treatment contrasts are shown in Figures 24, 25, and 26, for the three significant dependent variables (TC 1, TC 2, and LOC, respectively). The RMS means for the PTC combination are significantly larger than the placebo for the TC 1 and the LOC dependent variables and than the TC combination for the TC 1, TC 2, and LOC dependent variables, which indicated a performance decrement as a result of the PTC combination.

The results of the univariate analyses indicated a significant flight main effect for all 6 dependent variables. The RMS means and SE of the means for the 5 post-drug flights for the ALT 2 and LOC dependent variables are shown in Figures 28 and 29, respectively. For both ALT 2 and LOC there is, essentially, a monotonic increase in the RMS means from flight 2 to flight 6; although the differences are statistically reliable, they are small. The univariate analyses also indicated a significant treatment (drug) x flight interaction for 4 of the 6 dependent variables (ALT 1, ALT 2, TC 1, and LOC). To further examine the time course of the treatment effect, the RMS means and SE of the means were computed for each of the 3 treatment (drug) conditions for the 5 post-drug flights for the ALT 2 and the LOC dependent variables (Fig. 30 and Fig. 31, respectively). Both of these dependent variables had a significant flight main effect and a significant treatment (drug) x flight interaction; however, the treatment (drug) main effect was not significant for

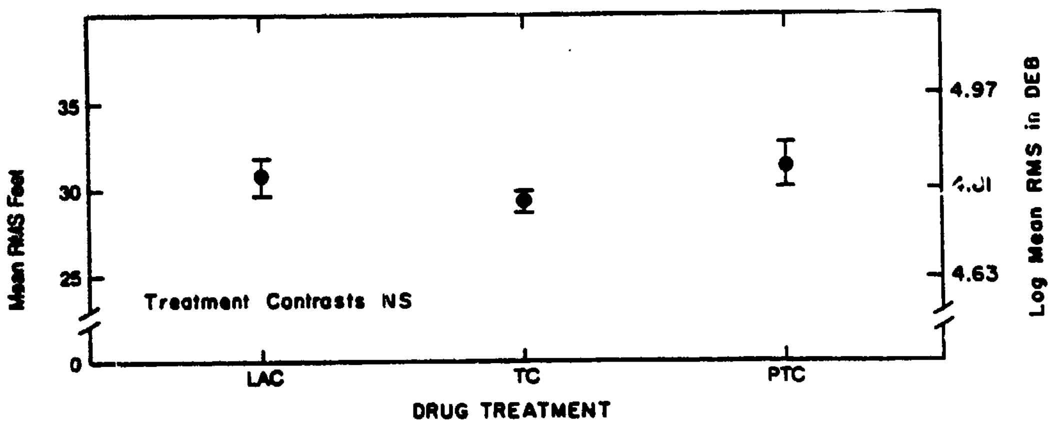

Figure 22. RMS means and standard error of the means by each combination antiemetic drug treatment for ALT 1 variable (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

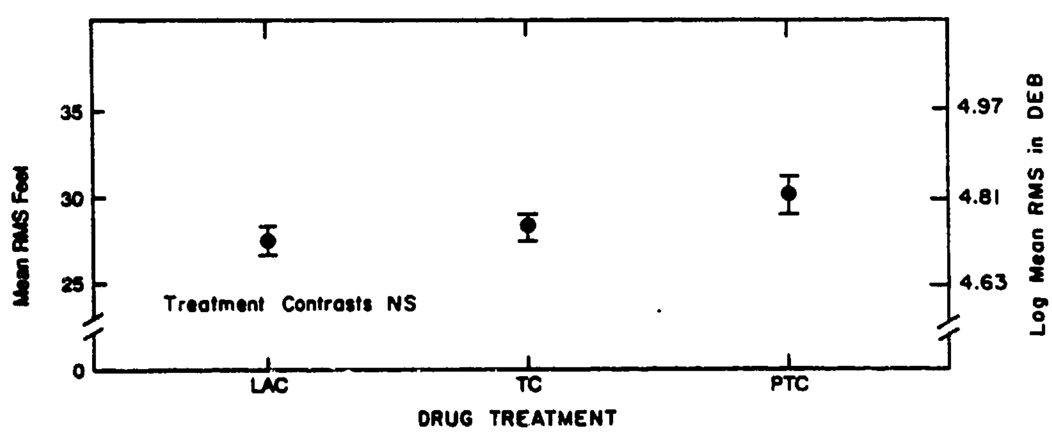

Figure 23. RMS means and standard error of the means by each combination antiemetic drug treatment for ALT 2 variable (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

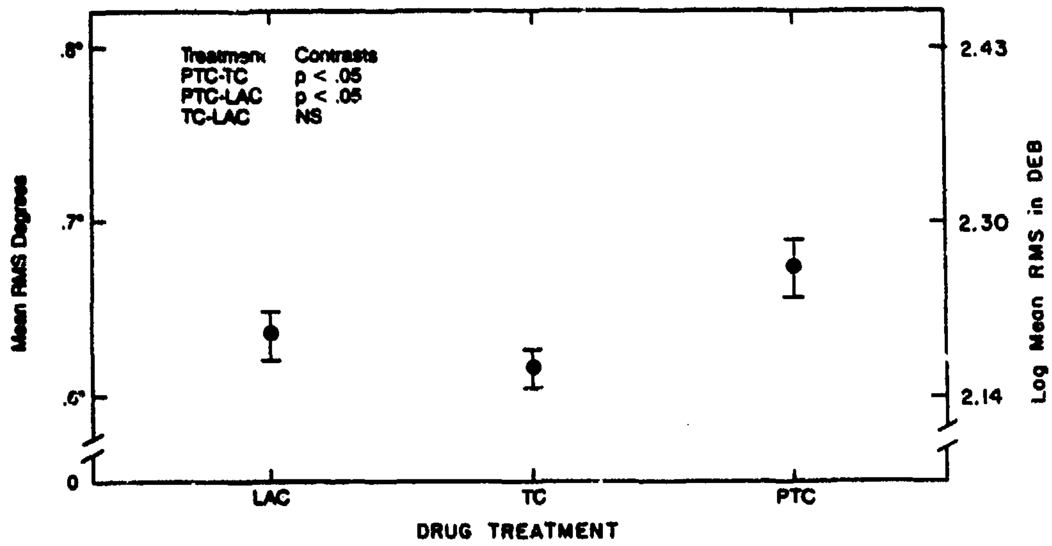

Figure 24. RMS means and standard error of the means by each combination antiemetic drug treatment for TC 1 variable (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

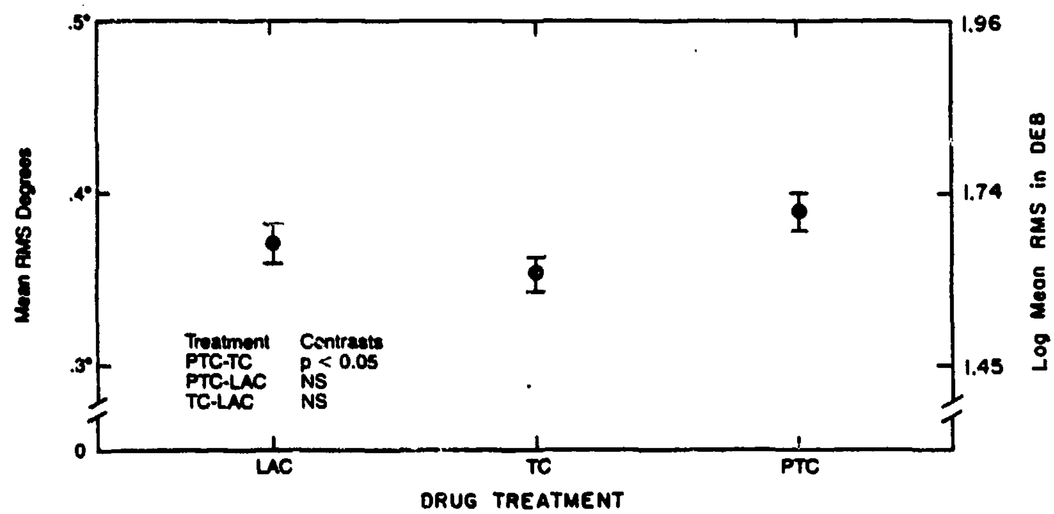

Figure 25. RMS means and standard error of the means by each combination antiemetic drug treatment for TC 2 variable (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

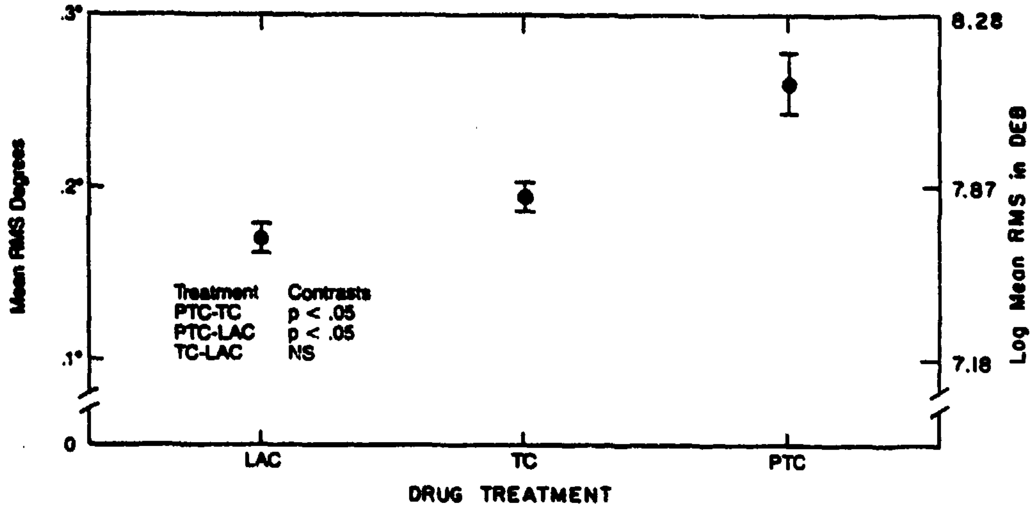

Figure 26. RMS means and standard error of the means by each combination antiemetic drug treatment for LOC variable (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

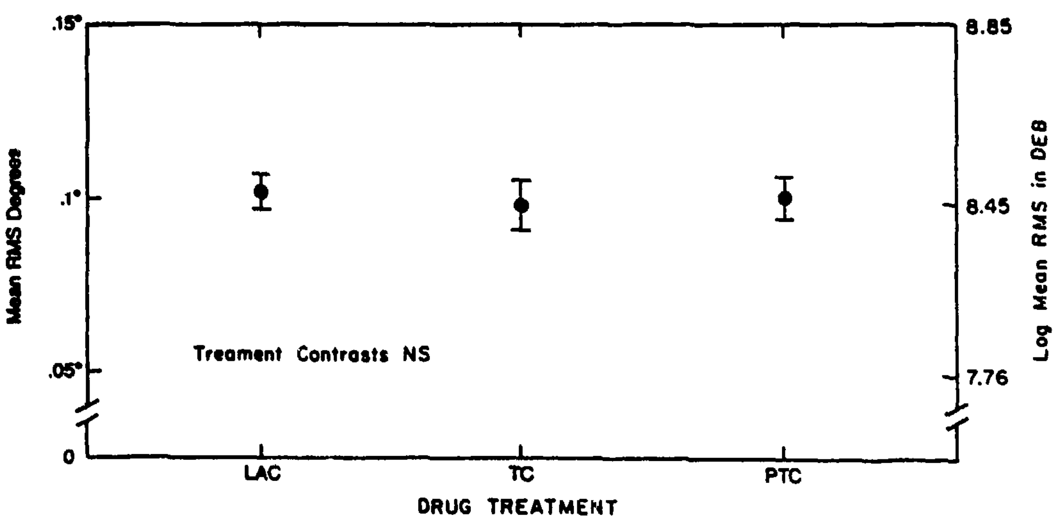

Figure 27. RMS means and standard error of the means by each combination antiemetic drug treatment for GLS variable (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

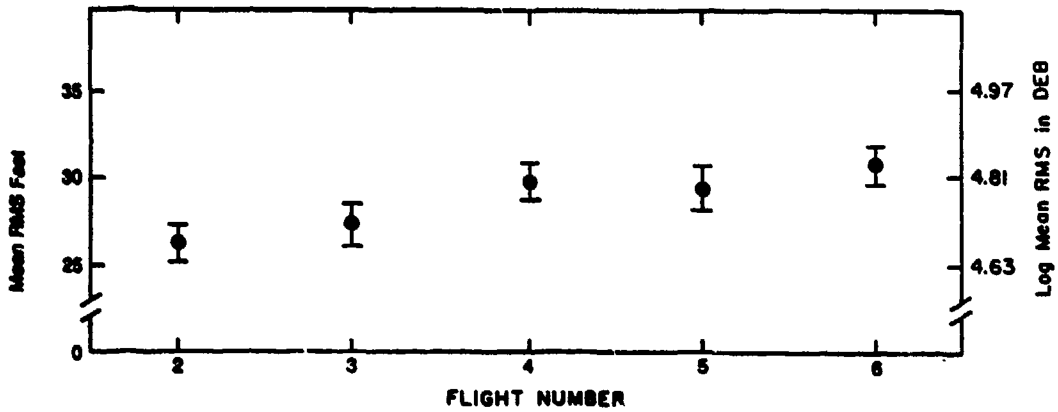

Figure 28. RMS means and standard error of the means by each post-drug flight for ALT 2 variable in the combination antiemetic drug experiment (3 experimental sessions, 12 subjects), N = 36.

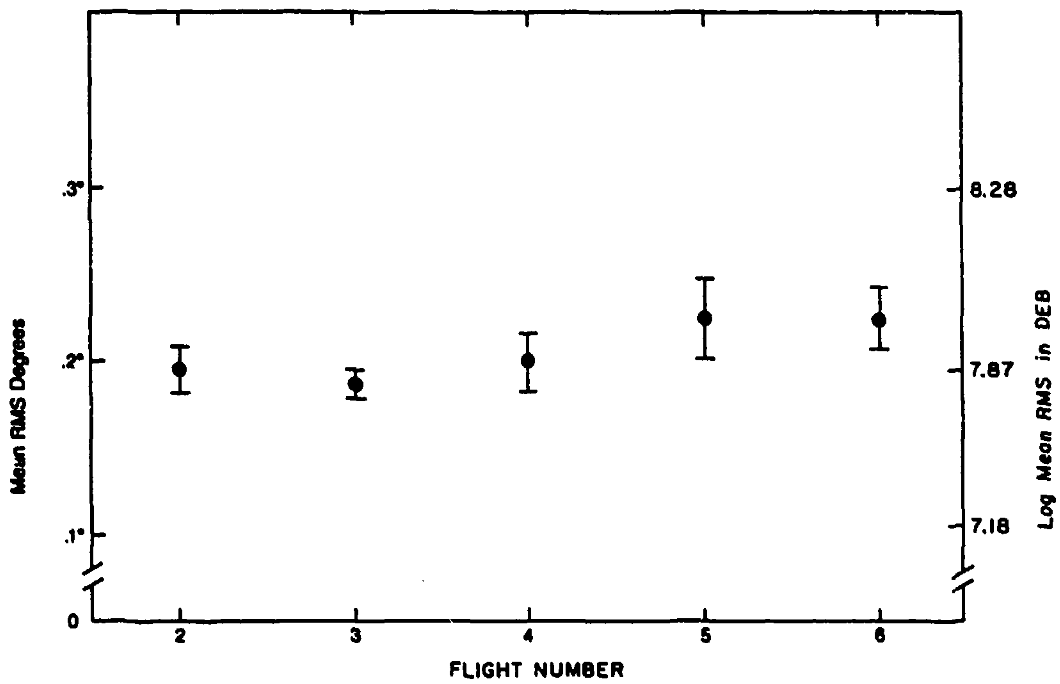

Figure 29. RMS means and standard error of the means by each post-drug flight for LOC variable in the combination antiemetic drug experiment (3 experimental sessions, 12 subjects), N = 36.

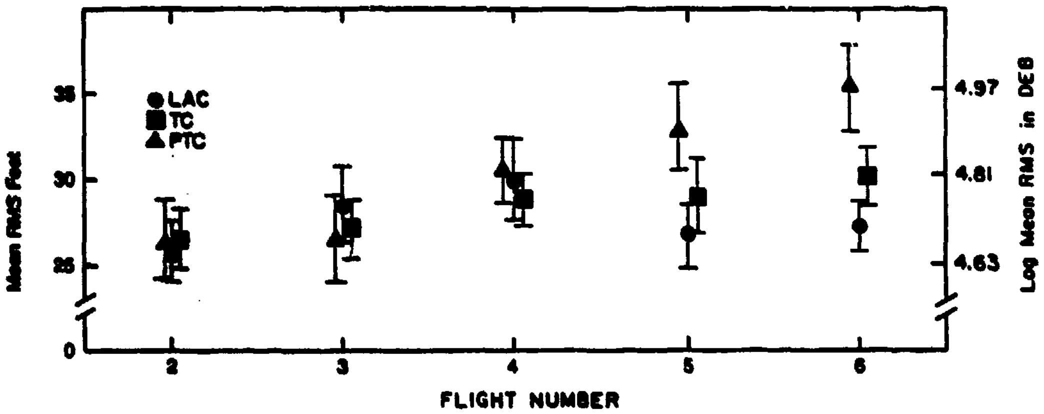

Figure 30. RMS means and standard error of the means by each post-drug flight for ALT 2 variable for each antiemetic drug (12 subjects), N = 12. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

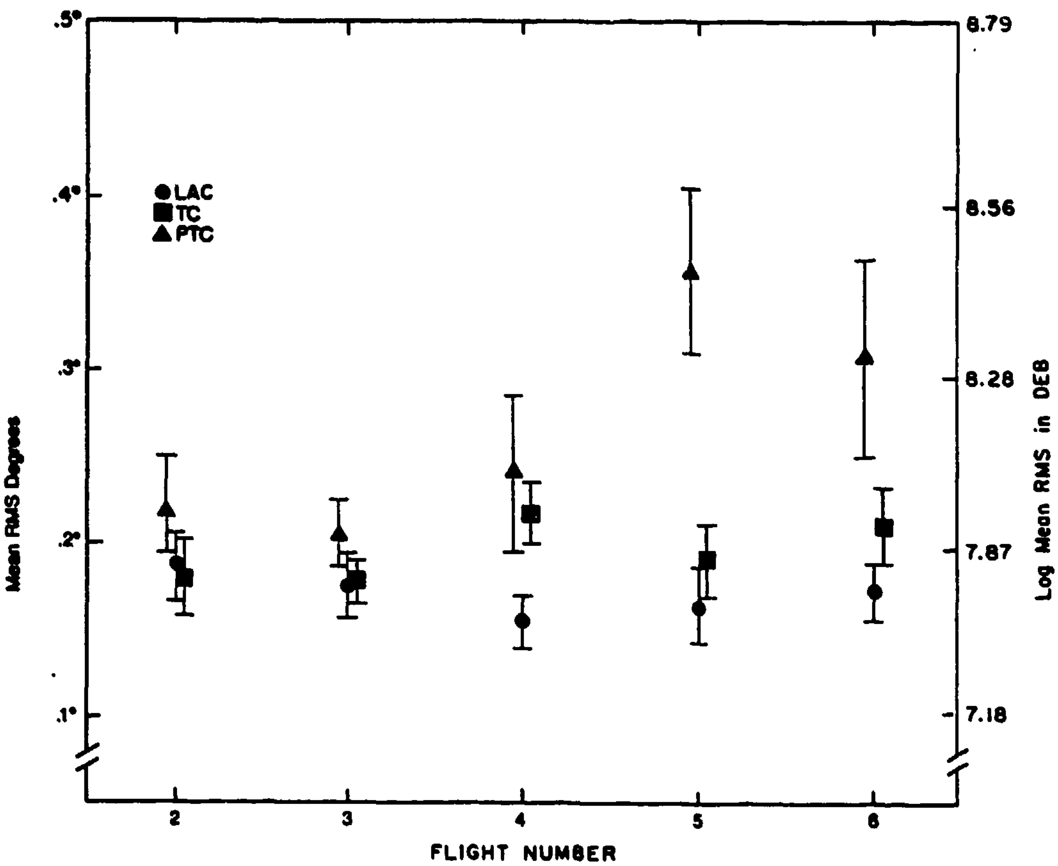

Figure 31. RMS means and standard error of the means by each post-drug flight for LOC variable for each antiemetic drug (12 subjects), N = 12. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

ALT 2, but was significant for LOC. Examination of Figure 30 (ALT 2) indicates a monotonic increase for PTC and random variability with no consistent pattern for the lactose (placebo) and the TC combination. Examination of Figure 31 (LOC) indicates a similar random variability with no consistent patterns for the placebo and TC conditions. The SE of the means for the localizer for the PTC condition showed a substantial increase for flights 4, 5, and 6. The RMS means for PTC are also larger for these flights with the peak value occurring during flight 5.

To examine the treatment effects for each post-drug flight, ANOVAs were computed for each of the 6 dependent variables. The results of these analyses are summarized in Table 7. Except for the GLS dependent variable for flight 2, there were no significant treatment effects for flights 2 and 3. The LOC variable was significant for flights 4, 5, and 6; ALT 2 and TC 1 were significant for flights 5 and 6; and TC 2 for flight 6. The ALT 1 was not significant for any of the 5 post-drug flights. Tukey's Studentized Range Tests were computed between each treatment condition for the 6 primary task dependent variables for the 5 post-drug flights. The results of these tests are summarized in Table 8. Examination of these data indicated that the performance decrements were due to the differences between the PTC combination and one or both of the other 2 treatment conditions (placebo and/or the TC combination). The difference between the TC combination and the placebo was significant for only one test (LOC for flight 4).

TABLE 7. SUMMARY OF THE F-STATISTICS FOR THE TREATMENT EFFECT FOR THE 6 PRIMARY TASK DEPENDENT VARIABLES FOR THE 5 POST-DRUG FLIGHTS

Primary task dependent variable	Flight*				
	2	3	4	5	6
ALT 1	NS	NS	NS	NS	NS
ALT 2	NS	NS	NS	5.37[a]	6.38[b]
TC 1	NS	NS	NS	10.36[c]	8.22[b]
TC 2	NS	NS	NS	NS	4.34[a]
LOC	NS	NS	8.06[b]	22.99[c]	5.83[b]
GLS	3.54[a]	NS	NS	NS	NS

[a]$p < .05$ [b]$p < .01$ [c]$p < .001$ NS = Not Significant

*$F(2,18)$.

TABLE 8. SUMMARY OF TUKEY'S STUDENTIZED RANGE TEST BETWEEN EACH TREATMENT FOR THE 6 PRIMARY TASK DEPENDENT VARIABLES FOR THE 5 POST-DRUG FLIGHTS

Primary task dependent variable	Flight				
	2	3	4	5	6
ALT 1	NS	NS	NS	NS	NS
ALT 2	NS	NS	NS	PTC-PCB	PTC-PCB
TC 1	NS	NS	NS	PTC-PCB PTC-TC	PTC-PCB PTC-TC
TC 2	NS	NS	NS	NS	PTC-TC
LCC	NS	NS	PTC-PCB TC-PCB	PTC-PCB PTC-TC	PTC-PCB
GLS	NS	NS	NS	NS	NS

NS = Not Significant

PTC = Promethazine hydrochloride, Thiethylperazine, and Cimetidine Combination
TC = Thiethylperazine, and Cimetidine Combination
PCB = Placebo

The reaction time data for the Sternberg Memory Search task (dual condition) for the 12 subjects for the 5 post-drug flights were used in an ANOVA to test the main effects of treatment (drug), flight, experimental session (column), group (row), response (hit-correct rejection), MSET, flight phase (hold-approach), and subject (nested within group). The data set had a total of 1432 observations. A summary table of the ANOVA results is included as Appendix D. An exact F-test, based on Wilks' criterion, was not significant for the treatment (drug) main effect. The main effects of flight, experimental session (column), response (hit-correct rejection), flight phase (hold-approach), and subject (nested within group) were all significant. Group and MSET were not significant. The treatment (drug) x flight interaction was significant as was the response (hit-correct rejection) x MSET interaction.

The same main effects except for flight phase (hold-approach) were tested for the Sternberg single task condition. Data from 12 subjects across 4 post-drug blocks of trials were used in an ANOVA. The data set had a total of 568 observations. A summary table of the ANOVA results is included as Appendix E. An exact F-test based on Wilks' criterion was not significant for the treatment (drug) main effect. The main effects of flight, experimental session, response (hit-correct rejection), MSET, and subject (nested within group) were significant. The treatment x flight interaction was significant.

The mean reaction times for the 3 treatment conditions were analyzed separately for the hold and approach phases of flight. The mean reaction time for the hold phase of flight for 12 subjects and 5 flights for the hit (true) and the correct rejection (false) conditions is shown in Figure 32. The same variables for the approach phase are shown in Figure 33. The reaction times for the approach condition are longer than the hold reaction times for both MSET 2 and MSET 4. As previously reported, the principal analysis indicated that there was no treatment main effect. The separate ANOVAs for the hold and approach flight phases confirmed this finding. MSET 4 hit (true) reaction times are greater than MSET 2 reaction times for both hold and approach phases of flight. These differences were not found for the correct rejection (false) condition. The ANOVAs were computed to test the significance of the differences. The analyses for both hold and approach indicated that MSET for the hit condition was significant. No significant difference for MSET was found for either hold or approach phase for the correct rejection condition. For both hold and approach, the reaction time difference between hit and correct rejection was about 200 ms.

The mean reaction times by set size for the single task Sternberg Memory Search task for the 3 treatment conditions are shown in Figure 34. Reaction times for hit (true) and correct rejection (false) are plotted separately. The mean reaction times for correct rejections are approximately 200 ms longer than for hit. In comparing the hold mean reaction times with the single task mean reaction times, the hold mean times are also approximately 200 ms longer than the single task reaction times. As reported before, MSET was significant for the Sternberg Memory Search single task condition. Separate ANOVAs indicate that MSET for both hit and correct rejection was significant for the single task condition.

Figure 35 shows mean reaction time by set size for the single task Sternberg Memory Search task for each experimental session. The reaction times for hit and correct rejection are plotted separately. As reported before, the ANOVA for the Sternberg single task resulted in a main effect for experimental session, $F(2,36) = 356$ ($P <= 0.039$). The longest reaction times occurred during the first experimental session (E 1) for both the hit and correct rejection condition. There was no orderliness in the function since experimental session 2 (E 2) showed faster reaction times than experimental session 3 (E 3). Further analyses using an ANOVA indicated that reaction time was significantly different for the experimental session for the correct rejection variable, but not for the hit variable.

As stated before, during the dual-task condition, the reaction times on the Sternberg Memory Search task were significant for experimental session. Figure 36 shows mean reaction time by set size for each experimental session with hits and correct rejections plotted separately. This figure represents the dual task hold phase of flight. An orderly decrease in reaction time can be seen with a significantly faster reaction time for session E3.

The absence of an experimental session main effect for the primary task variables was taken to indicate a learning plateau. However, learning might be reflected in increased residual capacity. The same primary task performance is accomplished with less effort. If this were the case, we should see improved performance on the secondary task. The orderly significant decrease in reaction time depicted in Figure 36 is congruent with

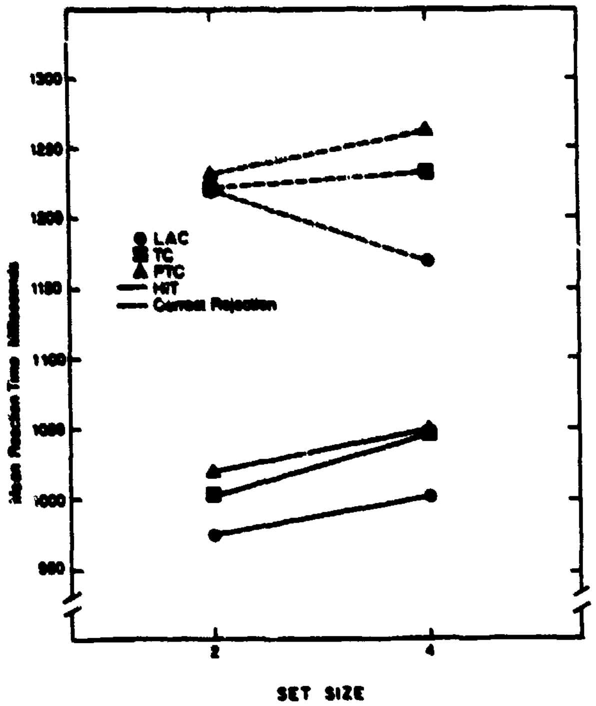

Figure 32. Mean reaction time by set size for dual task Sternberg Memory Search task for hold phase of flight (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

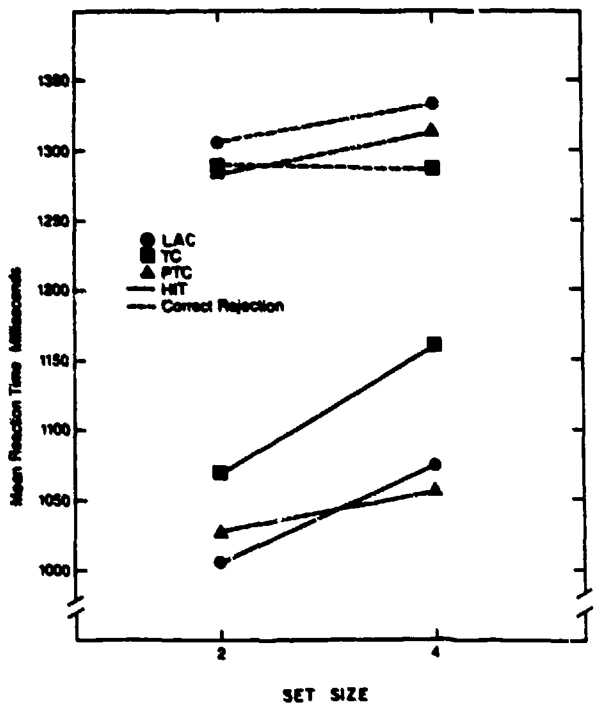

Figure 33. Mean reaction time by set size for dual task Sternberg Memory Search task for approach phase of flight (5 post-drug flights, 12 subjects), N = 60. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

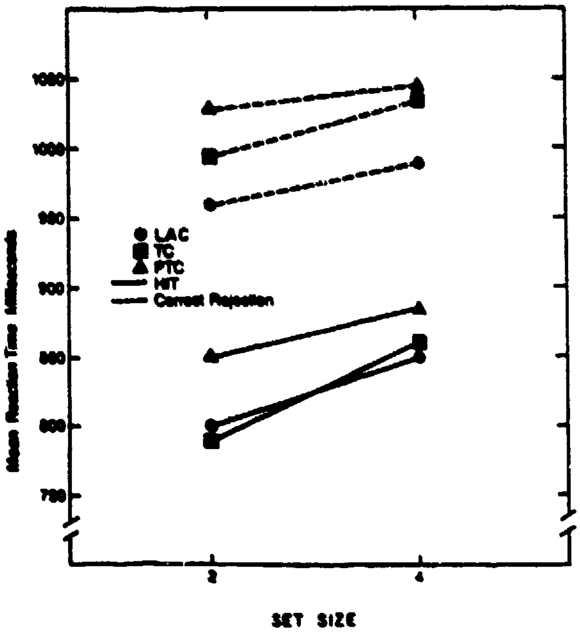

Figure 34. Mean reaction time by set size for single task Sternberg Memory Search task (4 blocks of trials, 12 subjects), N = 48. LAC = lactose placebo; TC = thiethylperazine and cimetidine combination; PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

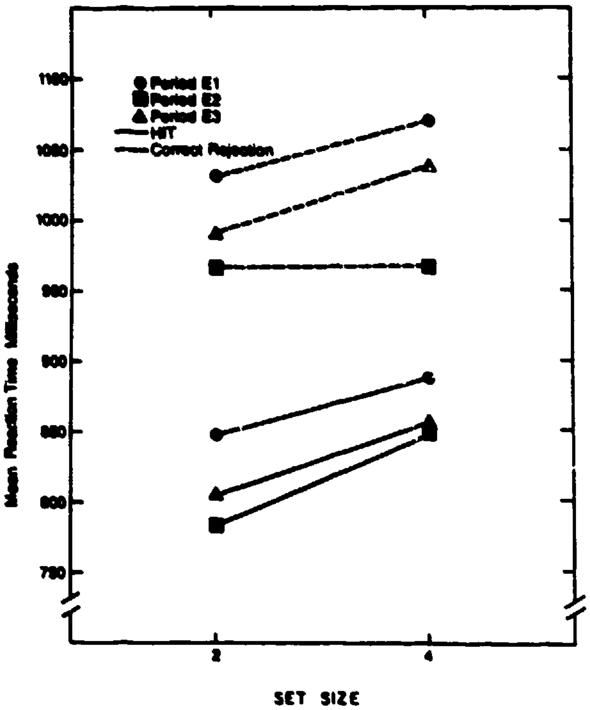

Figure 35. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false) and each experimental session (4 blocks of trials, 12 subjects), N = 48.

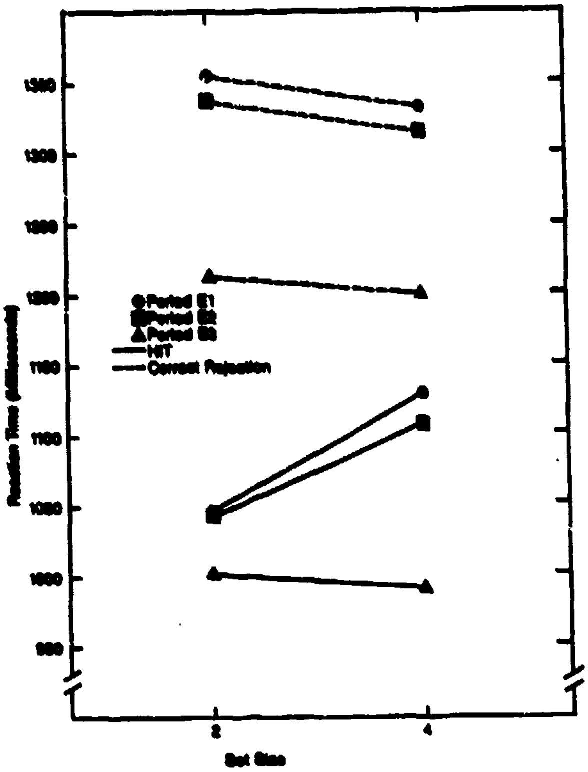

Figure 36. Mean reaction time by set size for dual task Sternberg Memory Search task averaged for the 3 drug conditions for hit (true) and correct rejection (false), and each experimental session (5 flights, 12 subjects), N = 60.

this hypothesis. An alternative explanation would be a general learning for the Sternberg task. However, the lack of orderliness seen in Figure 35 argues against this.

As reported before, the block of trials main effect for the ANOVA for the Sternberg single task condition was significant as was the block of trials x treatment interaction. The reaction times by set size for the single task Sternberg Memory Search task, for hit and correct rejection and each block of trials are shown in Figures 37 through 40. The mean reaction times by set size for single task Sternberg Memory Search task, for each block of trials averaged for all treatment conditions are shown in Figure 37. The hit and correct rejection trials are plotted separately. Reaction times systematically show an increase during the experimental session for both the hit and correct rejection conditions. The reaction times for the lactose (placebo) condition (Fig. 38) show no consistent patterns nor do the reaction times for the TC combination (Fig. 39). The reaction times for the PTC combination (Fig. 40), however, show a clear increase in reaction time throughout the experimental session for the hit condition. The same general trend is seen for the correct rejection with the exception of the reversal between blocks of trials 3 and 4.

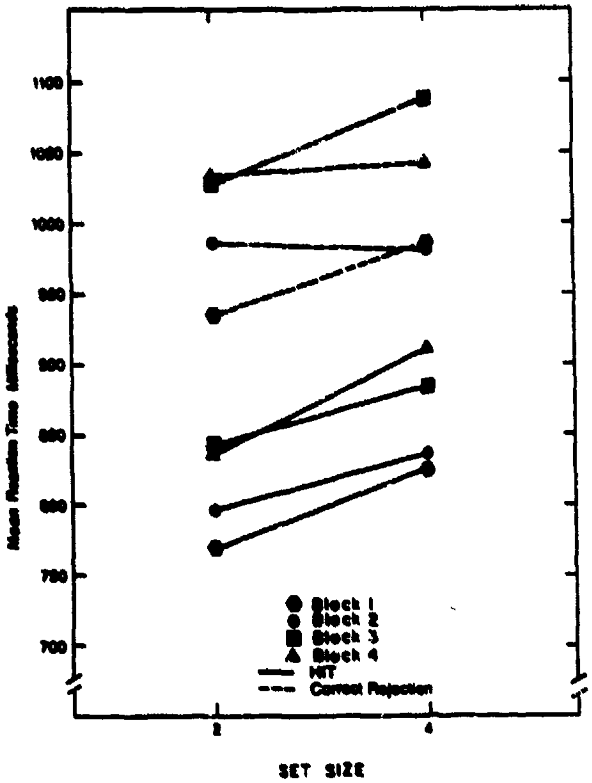

Figure 37. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false), for each block of trials (12 subjects, 3 drug conditions), N = 36.

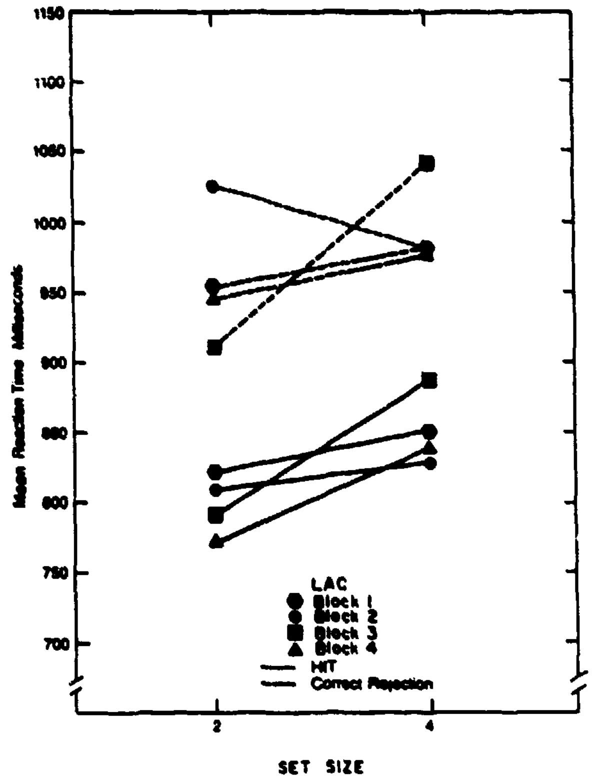

Figure 38. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false) and each block of trials (12 subjects), N = 12. LAC = placebo condition.

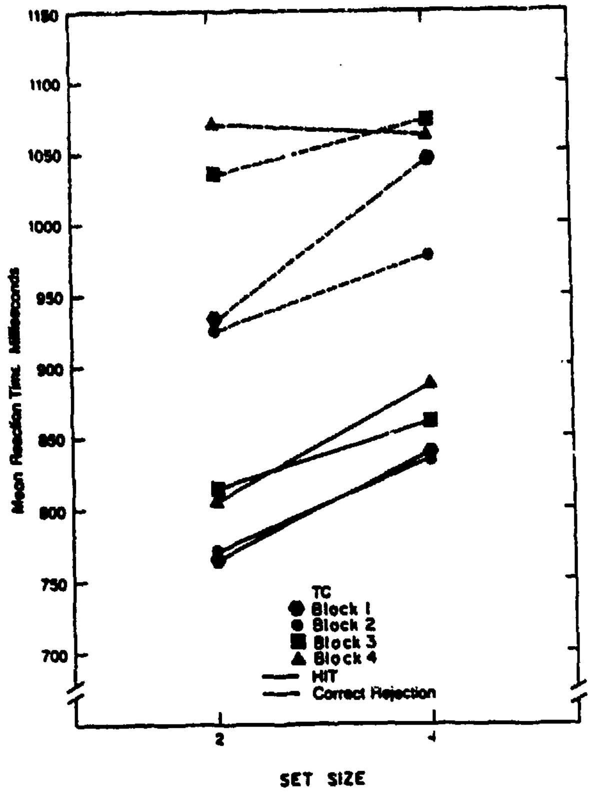

Figure 39. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false) and each block of trials (12 subjects), N = 12. TC = thiethylperazine and cimetidine combination.

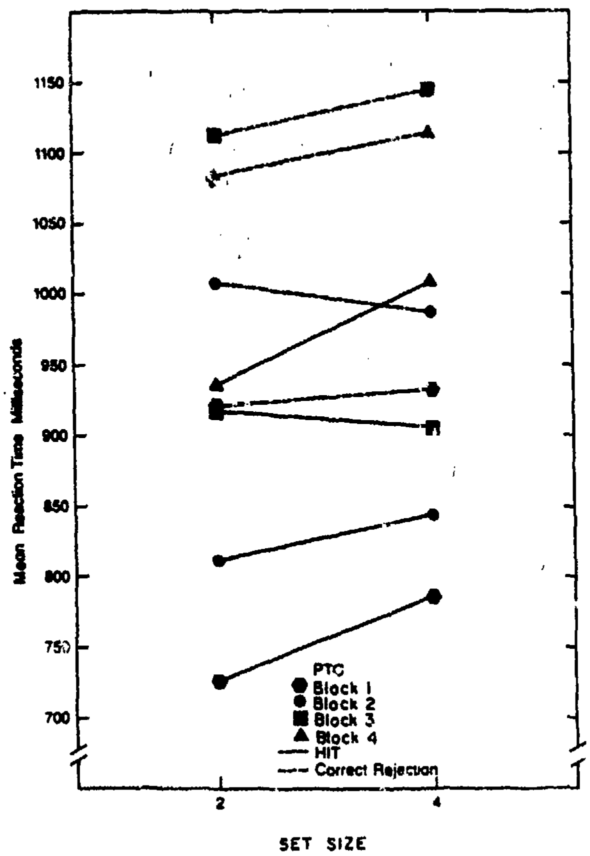

Figure 40. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false), and each block of trials (12 subjects), N = 12. PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

As reported before, the flight main effect for the hold phase of flight was significant as was the flight x treatment interaction. The mean reaction times by set size for the dual task Sternberg Memory Search task, for the hold flight phase, for the 5 post-drug flights are shown in Figures 41 through 44. Hit and correct rejection trials are plotted separately. The mean reaction times across all treatment conditions are shown in Figure 41. Reaction times for the hit condition show a consistent and orderly increase in reaction time throughout the experimental session for both MSET 2 and 4. The same general effect is seen for the correct rejection condition for MSET 2 (there is one reversal for flights 3 and 4), but not for MSET 4. The reaction times for both the placebo condition (Fig. 42) and the TC condition (Fig. 43) show no consistent pattern for either MSET 2 or 4 for either the hit or correct rejection. There is a consistent increase in reaction times for both MSET 2 and 4 for hit for the PTC drug condition (Fig. 44). The same general effect is seen for MSET 2 for correct rejection (there is a reversal for flights 3 and 4). Except for the reaction time on flight 2 being substantially lower than the other reaction times, there is no consistent pattern for MSET 4. The ANOVAs for hit and for correct rejection indicated that the MSET main effect was significant for hit, but not for correct rejection. The treatment x flight interaction, however, was significant for both variables as was the flight main effect.

Experiment IV

Peak BALs for Experiment IV were determined using both a Breathalyzer and whole-blood measurements. For the target BAL of 0.10% BAL, peak whole-blood measures ranged from .09% to .15%; the mean value was .12% and the median value was .115%. For a target value of .05%, whole-blood measurements ranged from .04% to .08% with a mean and median value of .06% BAL. For the Breathalyzer, the range for the target value of .10% was between .06% and .11% BAL with a mean of .09% BAL and a median of .10% BAL. For the target value of .05%, the range was between .02% and .08% BAL with a mean and median of .05% BAL. Although the Breathalyzer and whole-blood peak BAL values were different, the Breathalyzer indicated a peak BAL at the time of the second blood draw. Due to the variability of the Breathalyzer measurements within an experimental session, the mean whole-blood measurements will be used as the best indication of peak BAL.

A summary of the side effects for each BAL administered in Experiment IV is presented in Table 9. The symptoms were taken from the RN checklist and questionnaire, and from the subject symptom checklist which was completed after each of the 6 experimental flights comprising a single experimental session. The subjects' vital signs were also checked following each flight.

The flight data from the primary task were used to compute RMS values for the 6 dependent variables for each of the 3 experimental treatment conditions for each of the 12 subjects. The RMS scores were transformed using a log transformation. The log RMS scores for the 5 post-alcohol administration flights were used in a MANOVA to test the main effects of treatment (BAL), flight, experimental session (column), group (row), and subject (nested within group). The data set contained 177 of 180 possible observations; 3 observations were lost due to a computer malfunction. An F-test, based on Wilks' criterion, resulted in $F(12,26) = 3.79$ ($P<0.0021$) for the treatment

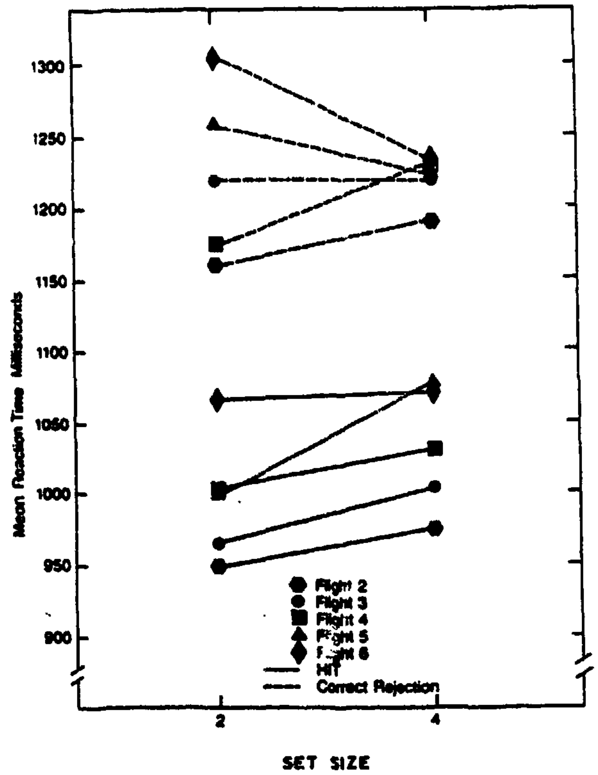

Figure 41. Mean reaction time by set size for dual task Sternberg Memory Search task averaged across the 3 drug conditions, for hit (true) and correct rejection (false), and each post-drug flight (12 subjects, 3 drug conditions), N = 36.

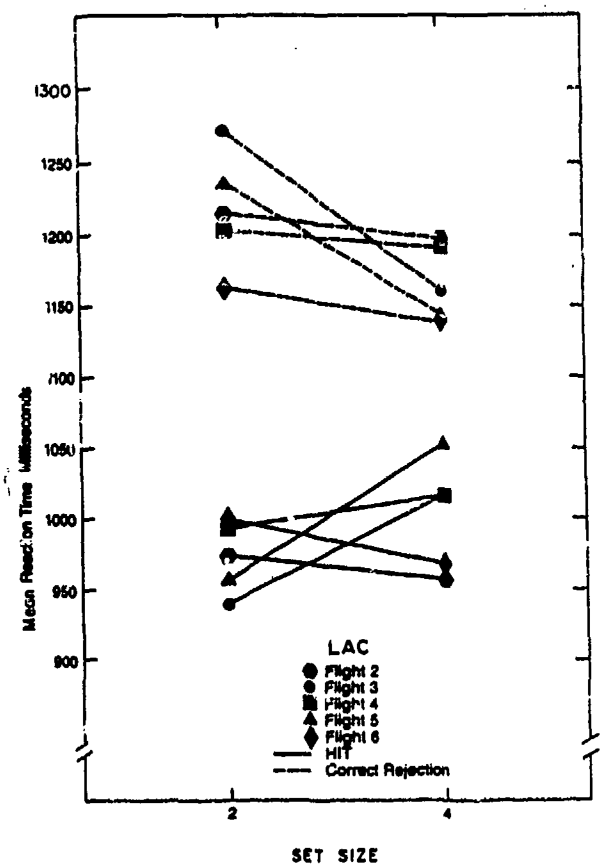

Figure 42. Mean reaction time by set size for dual task Sternberg Memory Search task for hold phase of flight, for hit (true) and correct rejection (false), and each post-drug flight (12 subjects), N = 12. LAC = placebo condition.

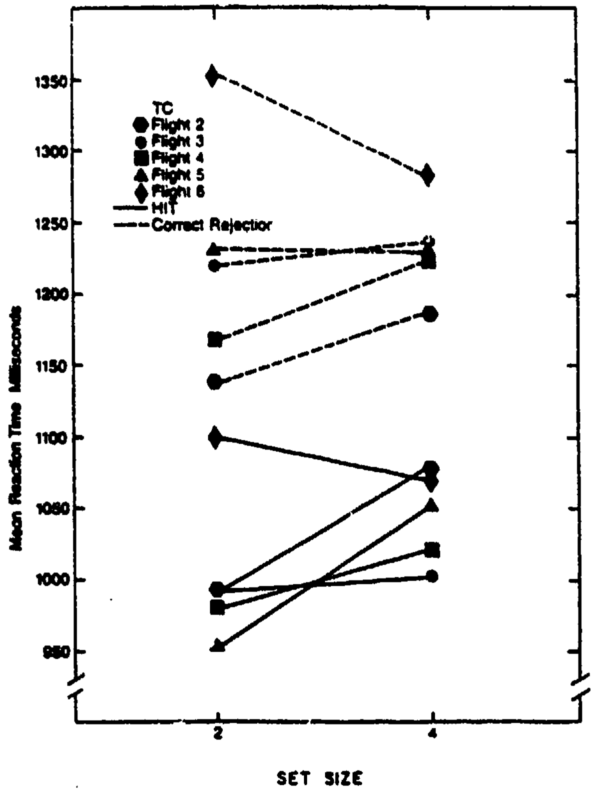

Figure 43. Mean reaction time by set size for dual task Sternberg Memory Search task for hold phase of flight, for hit (true) and correct rejection (false), and each post-drug flight (12 subjects), N = 12. TC = thiethylperazine and cimetidine combination.

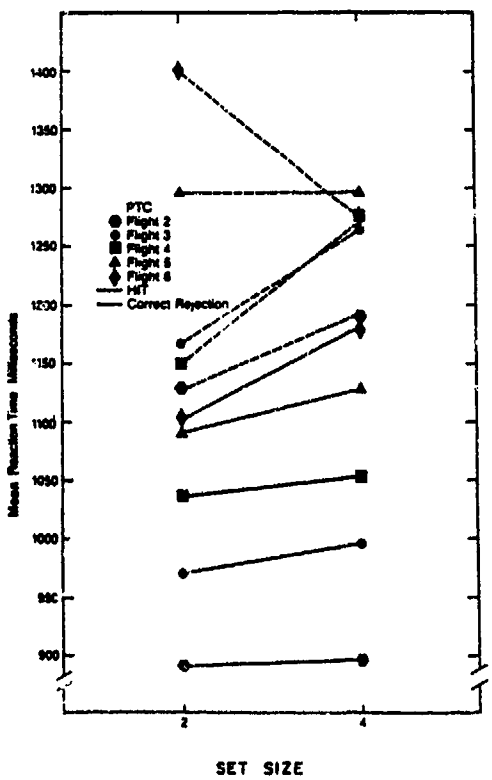

Figure 44. Mean reaction time by set size for dual task Sternberg Memory Search task for hold phase of flight, for hit (true) and correct rejection (false), and each post-drug flight (12 subjects), N = 12. PTC = promethazine hydrochloride, thiethylperazine, and cimetidine combination.

TABLE 9. SUMMARY OF SIDE EFFECTS FOR 3 BALs

	0 BAL	Medium BAL	High BAL
LA01	Very sleepy and fatigued--2 h sleep night before	Mild sleepiness and fatigue	Mild sleepiness, fatigue, mild blurred vision, mild slurred speech
LA02	Fatigued	Mild sleepiness	Mild sleepiness, fatigue, and transient headache
LA03	None	None	None
LA05	None	Mild sleepiness, lethargy and fatigue, some blurring of vision and slurring of speech	Vision blurred, speech slurred, salivating, sleepy and fatigued
LA06	Fatigued	Transient blurred vision, slurred speech, dizziness, mild sleepiness	Vision blurred, speech slurred, dizzy, nauseated sleepy, somewhat euphoric initially, subject unable to continue: emesis, vitals are normal
LA07	None	Transient euphoria and mild sleepiness	None
LA08	None	Transient euphoria	Nauseated, vision blurred, dizzy, numbness of extremities: Emesis. 20 min blackout, preceded by euphoria, unable to continue
LA09	None	Slight blurred vision and slurred speech--mildly sleepy and fatigued prior to treatment	Slight nausea, vision blurred, speech slurred, nervous

TABLE 9. SUMMARY OF SIDE EFFECTS FOR 3 BALs (cont'd)

	0 BAL	Medium BAL	High BAL
LA10	None	Slight dizziness, mild fatigue, and sleepiness	Slight dizziness and numbness of extremities, sleepy and fatigued
LA11	None	Mild fatigue and sleepiness	Speech slurred, mild euphoria
LA12	None	None	Sleepy, fatigued, dizzy, nauseated, slight headache
LA13	None	Subject reports sleepiness and fatigue prior to beginning session, no other symptoms	Subject reports sleepiness fatigue prior to beginning session, no other symptoms, normal questionnaire responses are not consistent
LA14	None	None	Vision blurred, speech slurred, dizziness and numbness of extremities
LA15	None	Mild transient euphoria, dizziness and numbness of extremities	Fatigued, sleepy, dizzy, numbness in extremities, speech slurred, vision blurred

(BAL) main effect. An F-test based on Wilks' criterion indicated that the flight, group, and experimental session main effects were not significant, and that none of the interactions were significant. An F-test based on Wilks' criterion for the subject (nested within group) main effect resulted in an $F(54,371) = 13.77$ ($P<0.0001$).

Univariate analyses were computed for the 6 primary task dependent variables. A summary of the analyses is presented in Appendix F. The analyses used MS for treatment (drug) x subject (nested within group) as an error term. For all 6 of the dependent variables, the results supported the findings of the MANOVA test of a significant treatment (BAL) main effect. The results of the ANOVAs indicated a significant flight main effect for the TC 2 dependent variable and significant treatment (BAL) x flight interaction for the TC 1 dependent variable. Tukey's Studentized Range Tests were computed between treatment pairs of the 3 BAL conditions for the 6 dependent variables. A summary of these tests is presented in Table 10.

TABLE 10. TUKEY'S STUDENTIZED RANGE TESTS BETWEEN THE 3 BLOOD ALCOHOL LEVEL CONDITIONS FOR THE 6 SIGNIFICANT DEPENDENT VARIABLES

Dependent variables	Treatment contrasts		
	O-M	O-H	M-H
ALT 1	NS	*	NS
ALT 2	NS	*	*
TC 1	NS	*	*
TC 2	*	*	*
LOC	NS	*	*
GLS	NS	*	*

*P = 0.05 O = Zero BAL H = High BAL
NS = Not Significant M = Medium BAL

Only one of the contrasts between the zero BAL and the medium BAL was significant (TC 2); all of the contrasts between the zero BAL and the high BAL were significant; and all of the contrasts except the ALT 1 contrast between the medium and the high BAL conditions were significant.

The RMS means and the standard error of the RMS means for the 3 BAL conditions averaged over the 12 subjects, and the 5 post-alcohol administration flights are shown in Figures 45 through 50 for each of the 6 dependent variables (ALT 1, ALT 2, TC 1, TC 2, GLS, and LOC, respectively). For all 6 dependent variables, the RMS means for the high BAL condition are significantly larger than the placebo (zero BAL); for all dependent variables except the ALT 1 variable, the RMS means for the high BAL condition are also significantly larger than the medium BAL condition. These results clearly indicate that the performance decrement was due primarily to the highest BAL condition. For the TC 2 variable, the medium BAL mean was significantly different from the zero BAL condition.

The RMS means and standard error of the means for the 3 BAL conditions for each of the 5 post-alcohol flights for TC 1 are shown in Figure 51. The effect of the high BAL condition is clear. The alcohol begins to have its effect during flight 3, the second post-alcohol administration flight; and the performance decrement remains essentially constant through flight 5. There is some performance recovery for flight 6, but the recovery does not appear to be complete. The means and standard error of the means for the TC 2 variable (Fig. 52) show a similar pattern to that seen for TC 1 except that the medium BAL condition is intermediate between the high BAL and the placebo for flights 3 through 6. A substantially different pattern is shown in Figure 53 (LOC variable). Although the same elevated mean RMS for the high BAL is apparent, the RMS mean for the placebo condition was larger than the medium BAL

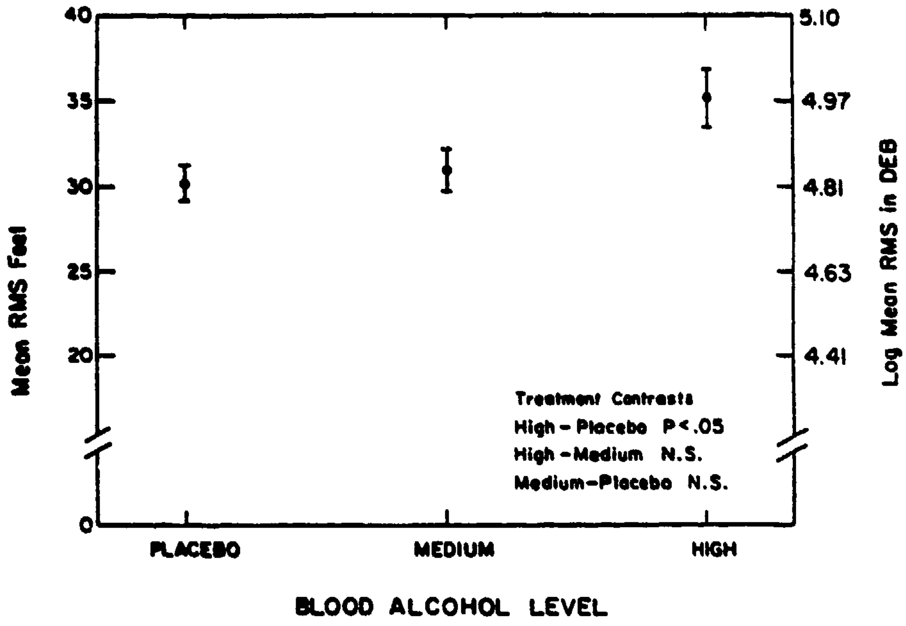

Figure 45. RMS means and standard error of the means by each BAL for ALT 1 variable (5 post-alcohol ingestion flights, 12 subjects), N = 60.

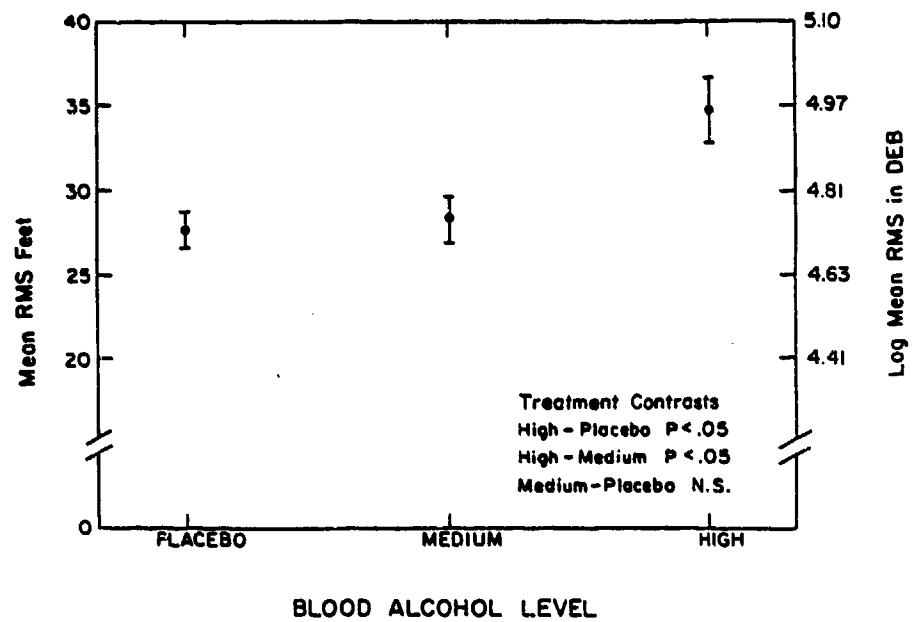

Figure 46. RMS means and standard error of the means by each BAL for ALT 2 variable (5 post-alcohol ingestion flights, 12 subjects), N = 60.

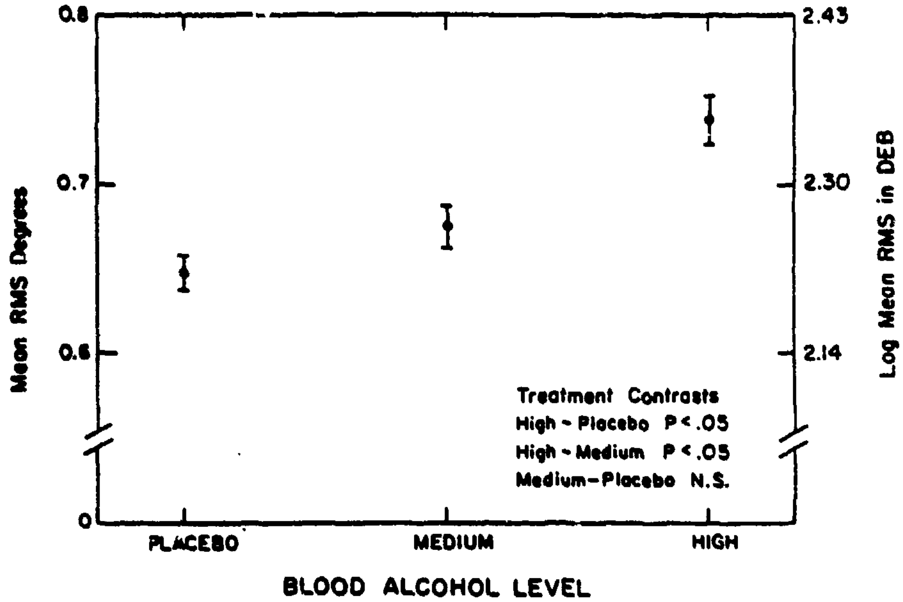

Figure 47. RMS means and standard error of the means by each BAL for TC 1 variable (5 post-alcohol ingestion flights, 12 subjects), N = 60.

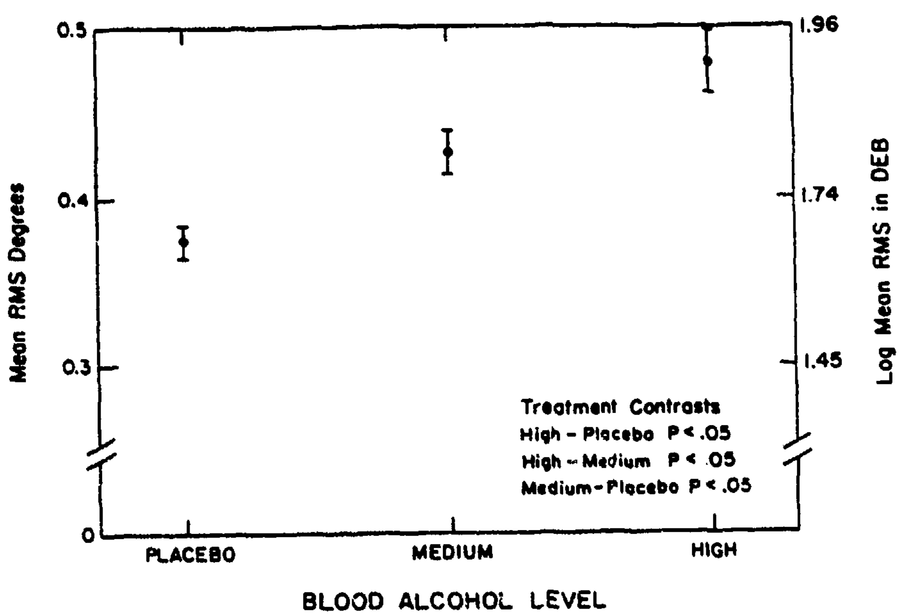

Figure 48. RMS means and standard error of the means by each BAL for TC 2 variable (5 post-alcohol ingestion flights, 12 subjects), N = 60.

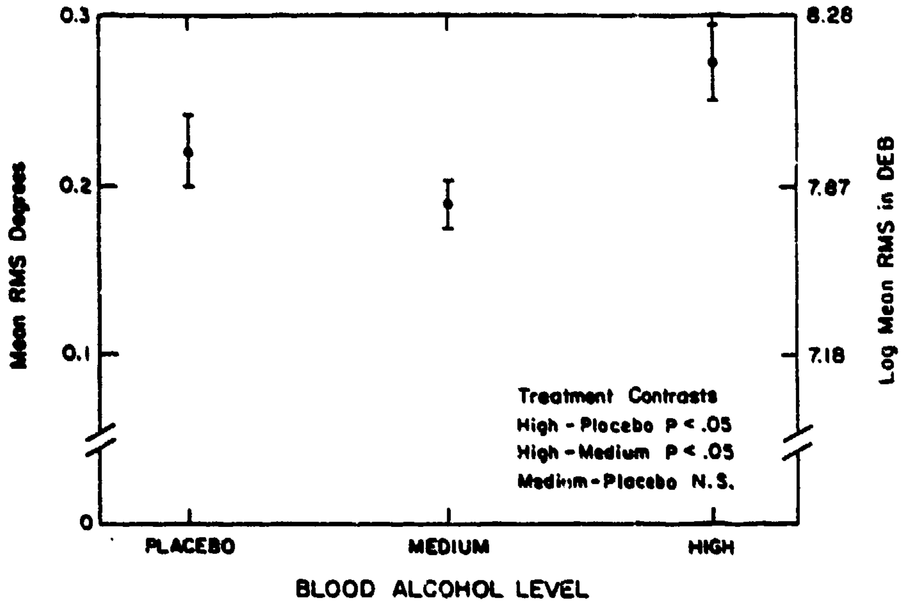

Figure 49. RMS means and standard error of the means by each BAL for GLS variable (5 post-alcohol ingestion flights, 12 subjects), N = 60.

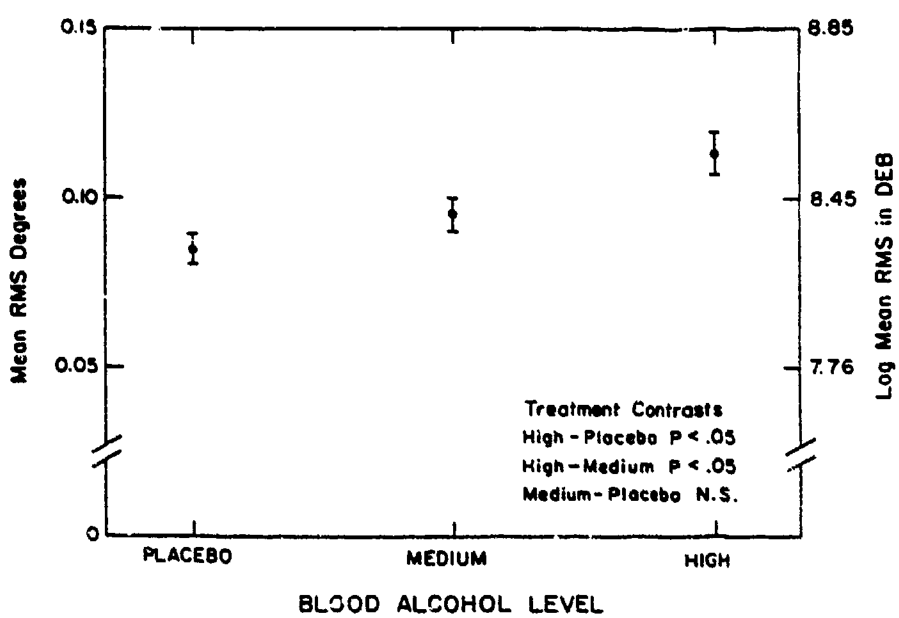

Figure 50. RMS means and standard error of the means by each BAL for LOC variable (5 post-alcohol ingestion flights, 12 subjects), N = 60.

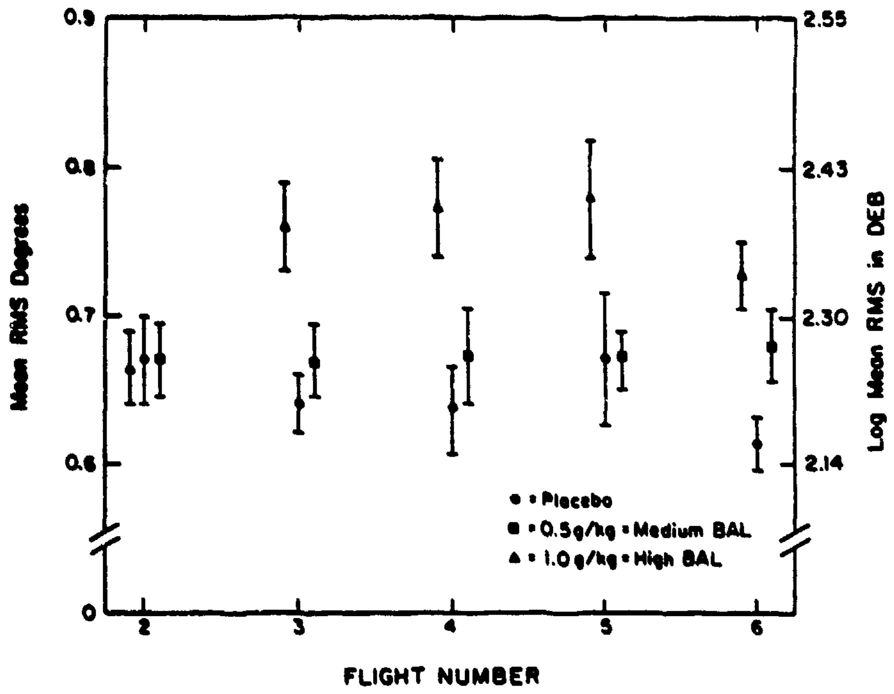

Figure 51. RMS means and standard error of the means by each post-alcohol ingestion flight for TC 1 variable, for each BAL (12 subjects), N = 12.

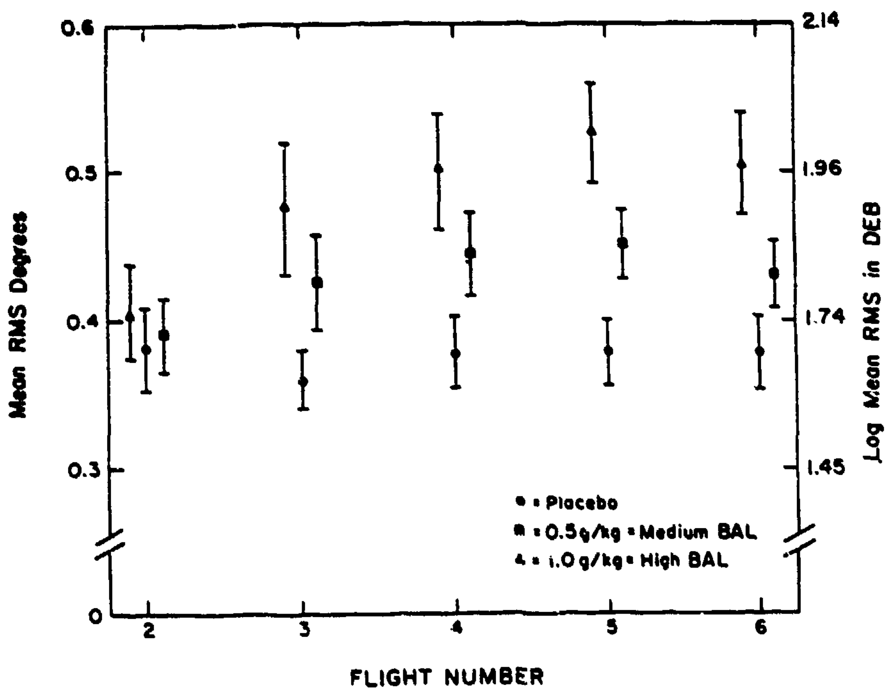

Figure 52. RMS means and standard error of the means by each post-alcohol ingestion flight for TC 2 variable, for each BAL (12 subjects), N = 12.

conditions. The mean and standard error of the means for the GLS dependent variable are shown in Figure 54. The increase in the high BAL means is apparent for flights 3 through 6.

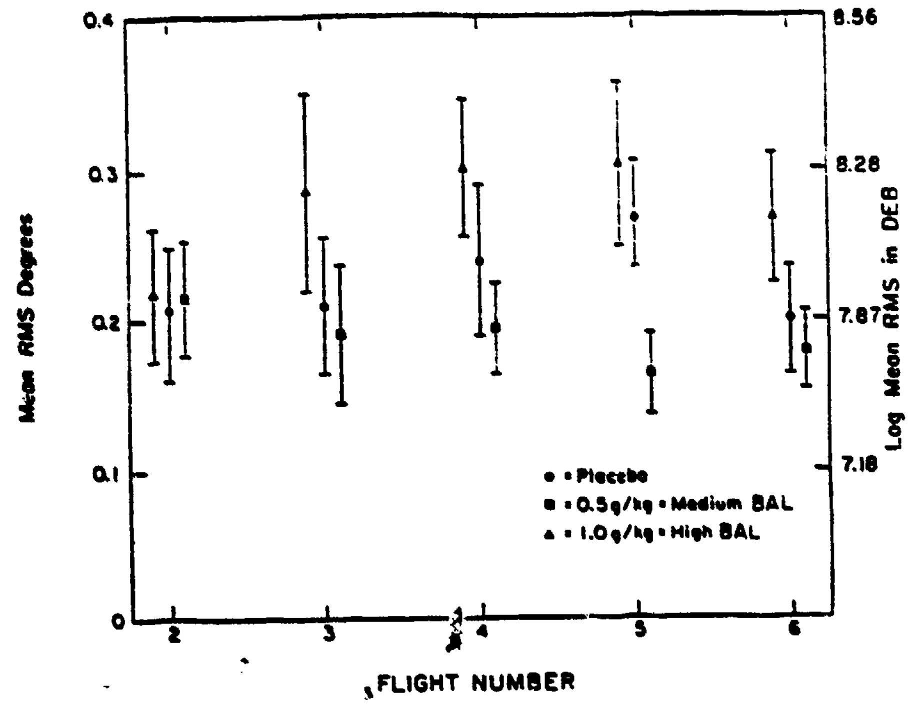

Figure 53. RMS means and standard error of the means by each post-alcohol ingestion flight for LOC variable, for each BAL (12 subjects), N = 12.

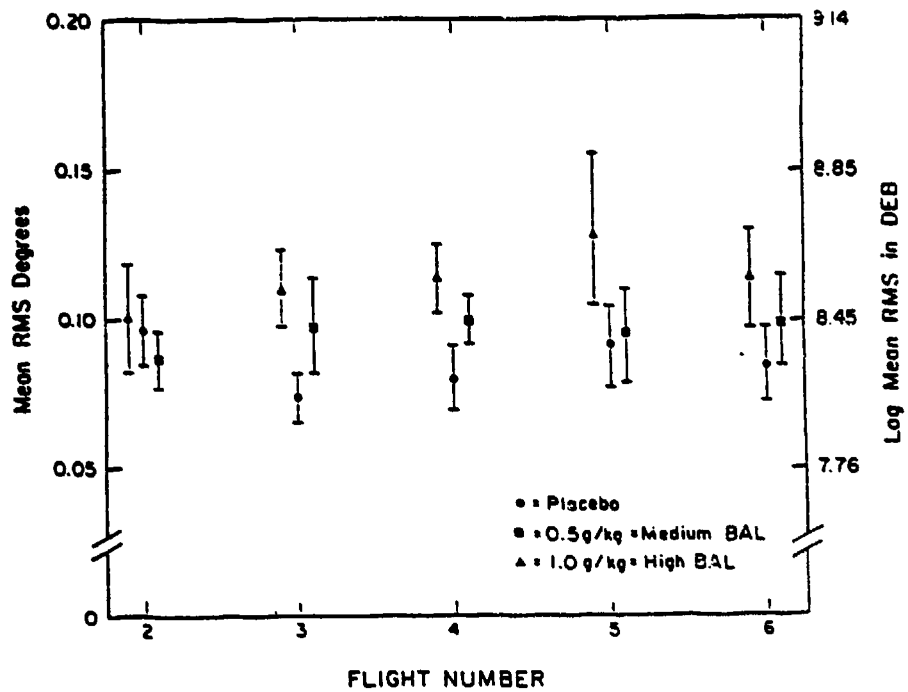

Figure 54. RMS means and standard error of the means by each post-alcohol ingestion flight for GLS variable, for each BAL (12 subjects), N = 12.

To examine the time course of the treatment (BAL) effects, ANOVAs were computed for each of the 6 dependent variables for each post-alcohol administration flight. The results of these analyses are summarized in Table 11. There were no significant treatment effects for flight 2. The TC 1 and TC 2 variables, however, were significant for the remaining 4 flights as was the GLS variable except for flight 5. All of the variables were significant on flight 5 except the GLS variable, and all but ALT 1 for flight 6. The ALT 2 and LOC variables were significant for the last 2 flights (flights 5 and 6), and ALT 1 was significant only for flight 5. Tukey's Studentized Range Tests were computed between each BAL condition for the 6 primary task dependent variables for the 5 post-alcohol administration flights. The results of these tests are summarized in Table 12. Examination of these data indicates that the performance decrements were due primarily to the differences between the high BAL condition and the other 2 BAL conditions (placebo and the medium BAL). The difference between the placebo and the medium BAL condition was significant for 3 contrasts, the medium vs. high BAL for 6 contrasts, and the placebo vs. high BAL for 13 contrasts.

The reaction time data for the Sternberg Memory Search task (dual condition) for the 12 subjects during the 5 post-alcohol administration flights were used in an ANOVA to test the main effects of treatment (BAL), flight, experimental session (column), group (row), response (hit-correct rejection), MSET, flight phase (hold-approach), and subject (nested within group). The data set had a total of 1373 observations out of 1432 possible observations. A summary table of the ANOVA results is included as Appendix G. An F-test was not significant for the treatment (BAL) main effect, $F(2,18) = 0.14$ $(P<0.63)$. The main effects of flight, response (hit-correct rejection), flight phase (hold-approach), and subject (nested within group) were all significant. Group, experimental session, and MSET were not significant. The treatment (BAL) x flight interaction was significant.

The reaction time (RT) means and the standard error of the means (MSET 2 and 4 combined) showed a monotonic increase from flight 2 through flight 5 for the hold flight phase for the high BAL condition. No other orderly relationships were observed for hold or approach phases of flight.

Since the difference between the reaction times for the hold and approach (dual task condition) phases was significant, the mean reaction times for the 3 treatment conditions for these 2 phases were analyzed separately. The mean reaction times for the holding phase of flight averaged over 12 subjects and 5 flights for the hit (true) and the correct rejection (false) conditions are shown in Figure 55. The same variables for the approach phase are shown in Figure 56. The reaction times for the approach phase (Fig. 56) are approximately 75 ms longer than the hold reaction times for the hold phase (Fig. 55) for both MSET 2 and MSET 4. During the hold phase for the hit trials, MSET 4 reaction times for each treatment (BAL) condition (Fig. 55) were greater than the reaction times for MSET, but not for the correct rejection condition. For both hold and approach, the reaction time difference between hits and correct rejections is about 200 ms. For the approach flight phase, no consistent pattern was apparent for the hit condition, but the correct rejection condition has the same pattern seen for the hold flight phase (Fig. 55). To examine these differences in more detail, separate ANOVAs were conducted for each response type (hit-correct rejection) for the hold and approach flight phases. The analyses showed for hit trials that MSET was

TABLE 11. SUMMARY OF THE F-STATISTICS FOR THE TREATMENT EFFECT (BAL) FOR THE 6 PRIMARY TASK DEPENDENT VARIABLES FOR THE 5 POST-ALCOHOL ADMINISTRATION FLIGHTS

Primary Task Dependent Variable	Flight*				
	2	3	4	5	6
ALT 1	NS	NS	NS	7.21[b]	NS
ALT 2	NS	NS	NS	4.57[a]	5.89[b]
TC 1	NS	9.30[c]	9.72[c]	4.08[a]	11.00[c]
TC 2	NS	4.64[a]	14.29[c]	10.79[c]	7.14[b]
LOC	NS	NS	NS	4.46[a]	6.29[b]
GLS	NS	5.94[b]	3.92[a]	NS	7.09[b]

[a]p = 0.05 [b]p = 0.01 [c]p = 0.001 NS = Not Significant
*F (2,18).

TABLE 12. SUMMARY OF THE TUKEY'S STUDENTIZED RANGE TEST BETWEEN EACH TREATMENT (BAL) FOR THE 6 PRIMARY TASK DEPENDENT VARIABLES FOR THE 5 POST-ALCOHOL ADMINISTRATION FLIGHTS

Primary task dependent variable	Flight*				
	2	3	4	5	6
ALT 1	NS	NS	NS	O-H	NS
ALT 2	NS	NS	NS	O-H M-H	O-H M-H
TC 1	NS	O-H M-H	O-H M-H	NS	O-H O-M
TC 2	NS	O-H	O-H O-M	O-H	O-H
LOC	NS	NS	NS	O-M M-H	M-H
GLS	NS	O-H	O-H	NS	O-H

*Alpha = 0.05 NS = Not Significant O = Zero BAL
M = Medium BAL
H = High BAL

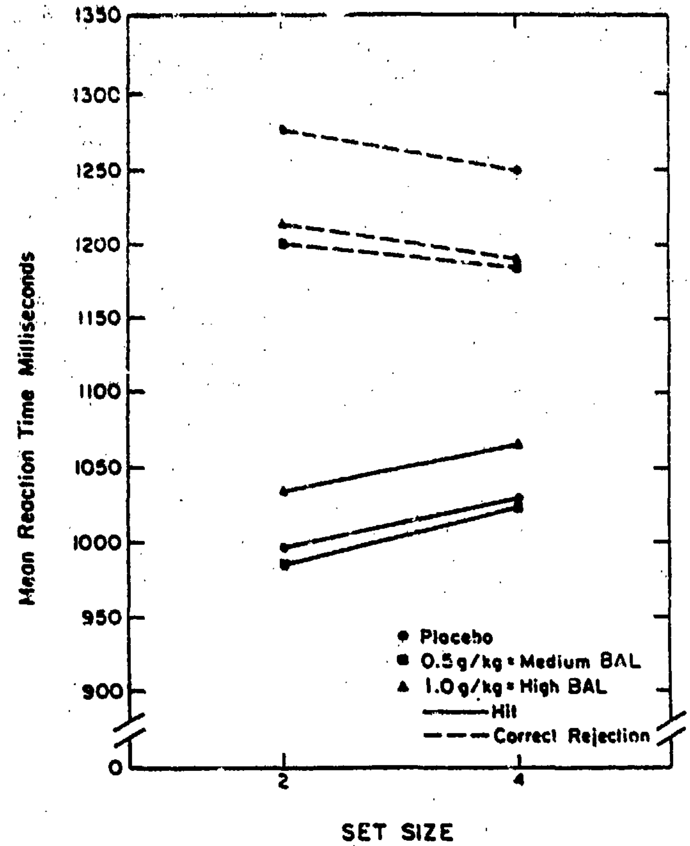

Figure 55. Mean reaction time by set size for dual task Sternberg Memory Search task for hold phase of flight, for nit (true) and correct rejection (false), and each BAL (5 flights, 12 subjects), N = 60.

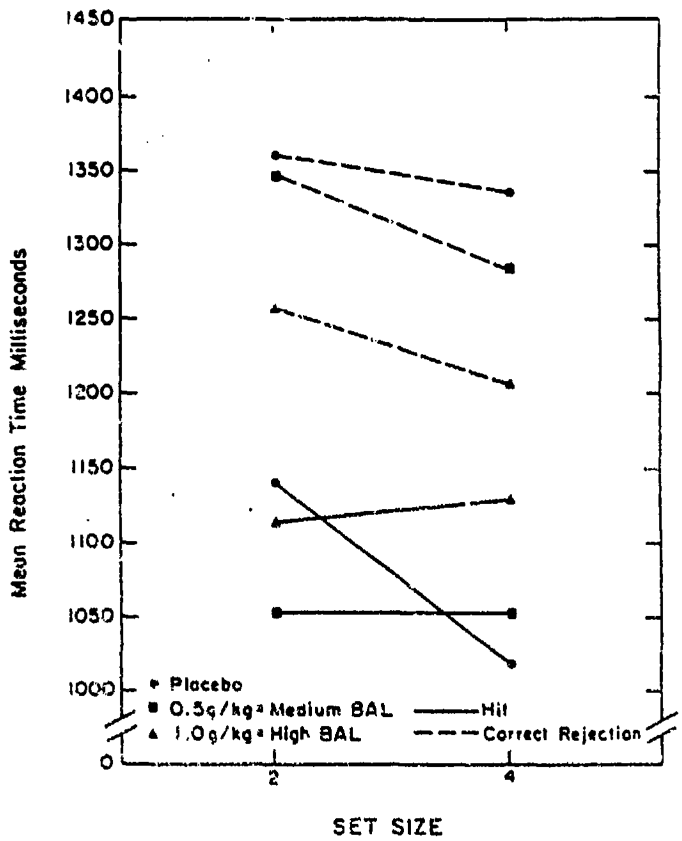

Figure 56. Mean reaction time by set size for dual task Sternberg Memory Search task for approach phase of flight, for hit (true) and correct rejection (false), and each BAL (5 flights, 12 subjects), N = 60.

significant for hold, but not for approach. Response time increased for those trials, but reaction times for correct rejection trials decreased as set size increased. During the approach phase, however, neither the main effect of set size nor the interaction with response type (hit-correct rejection) was significant.

The reaction time data for the Sternberg single task condition for the 12 subjects for the 4 post-alcohol administration trials were used in an ANOVA to test the same main effects tested in the dual task condition except for the flight phase (hold-approach). The data set had a total of 572 observations. A summary table of the ANOVA results is included as Appendix H. An F-test was not significant for the treatment (BAL) main effect, $F(2,18) = 0.88$ $(P<0.43)$. The main effects of flight, response (hit-correct rejection), MSET, and subject (nested within group) were significant. The flight x experimental session interaction was significant, but the treatment x flight and the flight x group interactions were not significant.

The mean reaction times, for the 3 treatment conditions for the single task Sternberg Memory Search task are shown in Figure 57. The mean reaction times for the correct rejection condition are approximately 200 ms longer than the hit condition, $F(1,9) = 307$ $(P<0.001)$, as was the case for the flight phases in the dual task condition. During the hold phase, the mean reaction times for the dual task (Fig. 55) are approximately 200 ms slower than the single task reaction times for all conditions, but 100 ms faster than the approach phase (dual task). As reported before, MSET was significant for the Sternberg single task condition. The ANOVAs indicated that MSET for both hit and correct rejection was significant for the single task condition.

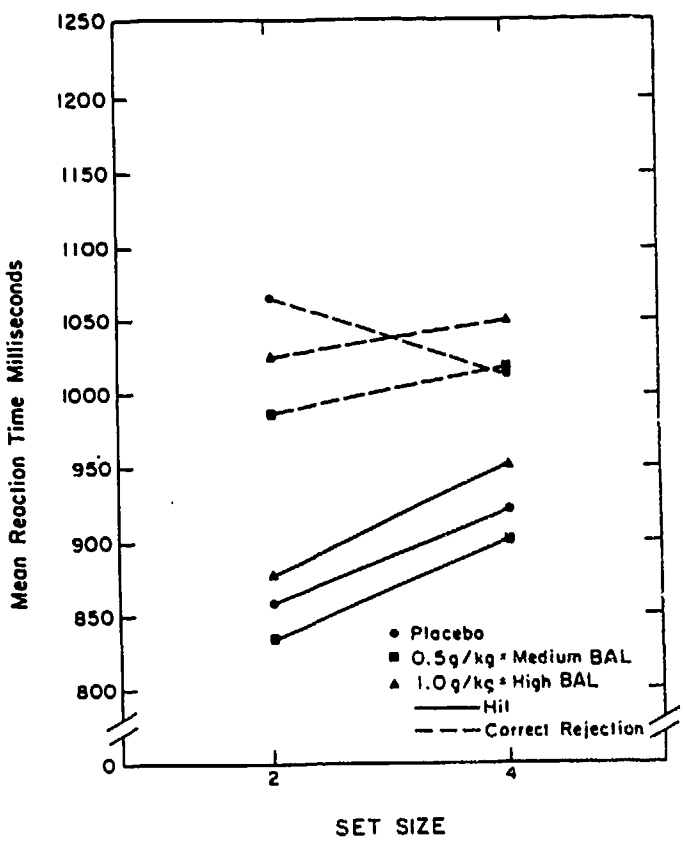

Figure 57. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false), and each BAL (4 blocks of trials, 12 subjects), N = 48.

As reported before, the block of trials main effect for the Sternberg single task condition was significant. The mean reaction times for each single task block of trials for hit and correct rejection, for MSET 2 and 4, averaged across all treatment conditions are shown in Figure 58. The difference is apparently due to the difference between the first block of trials and the 3 subsequent blocks of trials for both the hit and correct rejection conditions. The ANOVAs for hit and correct rejection indicated that the block of trials main effect was significant for both conditions.

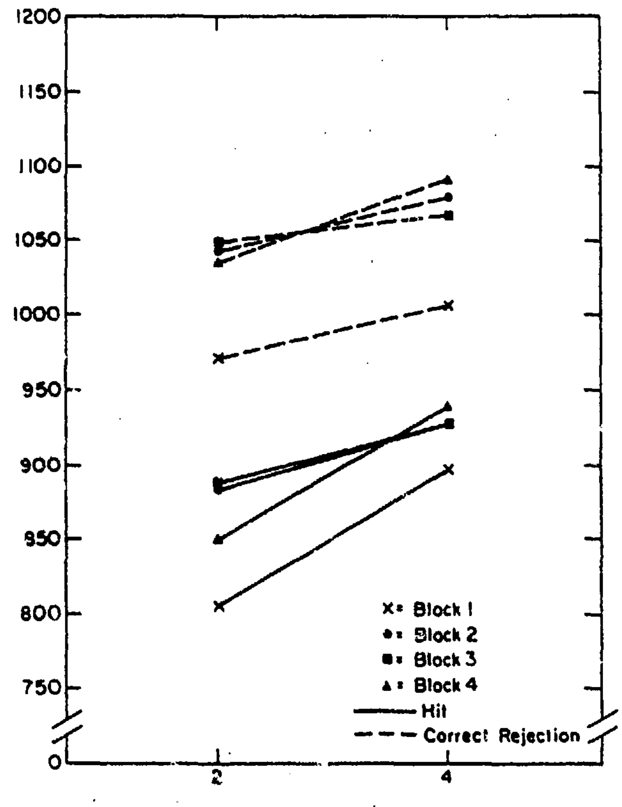

Figure 58. Mean reaction time by set size for single task Sternberg Memory Search task for hit (true) and correct rejection (false), and each block of trials (12 subjects, 3 BAL), N = 36.

To compare the relative performance decrements between the PTC antiemetic drug combination and the high BAL condition, the percentage decrements were computed between the PTC and the control for Experiment III and between the high BAL and the control for Experiment IV. Each primary task dependent variable was compared. The results of these computations are summarized in Table 13. For all dependent variables except for LOC, the comparisons between the high BAL and the control were substantially greater than for the PTC-control comparisons.

TABLE 13. COMPARISON OF RELATIVE PERFORMANCE DECREMENTS BETWEEN PTC VS. CONTROL AND HIGH BAL VS. CONTROL

	Percent Decrement	
Dependent Variable	PTC-Control	High BAL-Control
ALT 1	2%	18%
ALT 2	9%	26%
TC 1	6%	14%
TC 2	5%	30%
LOC	53%	23%
GLS	0%	38%

DISCUSSION

The results from Experiment I, the first alcohol experiment, provided calibration of the sensitivity of the automated performance methodology. The performance decrement on the primary task was significant for 3 of the 4 dependent variables at a measured median percent BAL of 0.082, but not for a median value of 0.038 or 0.014. These results are consistent with the findings of other investigators who used experienced pilots flying similar instrument flight tasks in a simulator (10,11). The results from the primary task data indicate that the methodology is appropriate for evaluating performance effects of toxic substances. The lack of significance of the MANOVA treatment main effect was probably due to the small number of subjects (7) in the study. A significant subject (nested within group) main effect suggests that, for future experiments involving the evaluation of toxic substances, the use of an experimental design in which each subject experiences all treatment conditions may be the most efficient design. Significant subject (group) effects have also been found for Experiments II, III, and IV, which further reinforces the need to use a within subjects, repeated measures design. No significant effect was found for the experimental session, indicating that the subjects' performances did not change over the course of the experiment as a result of practice on the primary task.

The results on the secondary task for Experiment I were not used since the malfunction of the random number generator introduced variability across experimental sessions that could neither be evaluated nor controlled. The subjects reported that they were able to anticipate the correct response from the repetitive pattern of three-letter sets.

The results from Experiment II, which involved evaluating the effects of promethazine hydrochloride, thiethylperazine, and cimetidine taken singly, indicate that all subjects were able to complete the primary task of flying

the aircraft as well as to maintain a high degree of accuracy on the secondary task. Comparable results were obtained from Experiment III, the combination antiemetic experiment. The Experiment II results showed a significant treatment main effect which indicated that antiemetic drugs produce a performance decrement. Further analysis of the 3 antiemetic drugs indicated that promethazine hydrochloride produced a performance decrement for 2 of the 4 dependent variables. The decrements were statistically reliable, but were smaller than decrements observed for the highest measured BAL (0.082%) in Experiment I. Thiethylperazine and cimetidine did not produce significant performance decrements when compared with control flights.

For Experiment II, performance on the LOC tracking task improved during the experiment, while the performance on the other 3 primary task dependent variables remained stable. Even though all subjects met the screening criteria for LOC tracking prior to the first experimental session, the results clearly indicate that the subjects' performance continued to improve with practice. The data suggest that 1 additional day of practice would probably have stabilized the baseline for this group of subjects. Therefore, additional training was provided, if required, for Experiments III and IV. The secondary task provided very little discrimination between the control and the antiemetic drugs. False reaction times were significantly different between control and cimetidine, but the false reaction times between the control and the other 2 drugs were not significant. No significant differences were found for either true reaction times or for accuracy.

Other investigators have reported performance decrements as a result of promethazine hydrochloride. Wood et al. (33) found that 25 mg oral or intramuscular (IM) administration of promethazine hydrochloride significantly increased errors on a computerized pursuit rotor task. These investigators reported the most pronounced error rate 4.5 h after drug administration for the oral dose.

Cooper and Mattsson (6) reported that promethazine hydrochloride increased the ED_{50} for radiation-induced emesis in dogs to 402 rad compared to 170 rad in control dogs. Thiethylperazine increased the ED_{50} to 320 rad and cimetidine increased the threshold to 331 rad. To determine the ED_{50} level of radiation-induced emesis, Mattsson et al. (1) administered, to dogs, lower doses of promethazine hydrochloride (13.92 mg/m^2) and thiethylperazine (5.57 mg/m^2) and higher doses of cimetidine (167 mg/m^2). Drug/body surface (mg/m^2) was used in an attempt to equate the different body sizes of dogs vs. humans. The doses chosen represented the following doses in a 70 kg human, which are the commonly prescribed human doses: 25 mg promethazine hydrochloride, 10 mg thiethylperazine, and 300 mg cimetidine. These drugs were administered singly and in combination. The results indicated that, of the 3 drugs administered singly, only thiethylperazine was statistically more effective in increasing the radiation threshold compared to the control group (1,7). The equivalent levels of the 3 antiemetic drugs used by Mattsson et al. (1) were used in our Experiments II (singly) and III (in combination) to determine the performance effects of the drugs in pilots. Since thiethylperazine produced no significant performance decrements and has been shown to be effective in increasing the radiation-induced emesis threshold, the results from Experiment II suggest that thiethylperazine should be used if a single drug is to be administered to prevent radiation-induced emesis in aircrew members.

Mattsson et al. (1) found that thiethylperazine increased the radiation-induced emesis threshold in dogs to 405 rad compared to 258 rad for untreated controls. The TC combination further increased the threshold to 446 rad and the PTC combination increased the threshold to 478 rad. They also found that the standard deviation of the PTC combination was smaller than any of the other treatments. None of the 3 antiemetic drugs administered either singly or in combination caused the dogs to be refractory to radiation emesis. Thiethylperazine, the TC combination, and the PTC combination significantly increased the threshold, but an emesis threshold still existed. Since combinations of drugs increased the emesis threshold and reduced variability, Mattsson et al. (1) interpreted these findings as evidence that different populations of receptors for emesis were being brought under control. The results from our Experiment III indicated that the TC combination was not different from the control condition for the primary task (flying the simulator). The PTC combination, however, was significantly different from the control. The differences were observed for 3 of the 6 dependent variables (the 2 turn rate control variables and the LOC tracking variable). Further analysis indicated that all of the differences occurred during the last 3 flights which occurred at 1:55 h, 2:35 h, and 3:15 h post-drug administration. There was a flight main effect, but it is not considered important for this investigation. The results of Experiment III indicate that the TC combination can be used without any flight performance degradation. While the PTC combination offers the greatest protection against emesis (about 7% over the TC combination), there is a flight performance decrement as the result of adding promethazine hydrochloride to the TC combination. The operational trade-off is clear. The use of PTC increases the emesis threshold, but results in a statistically reliable performance decrement, while the use of the TC combination results in a lower emesis threshold but produces no performance decrement.

The Sternberg Memory Search task was included as a secondary task with the expectation that it would not only use any available residual capacity after the pilots performed the primary task, but that it would also be diagnostic in terms of the locus of any performance decrement. It was anticipated that the Sternberg task data would be useful in determining whether the performance decrements were related to perceptual and cognitive processes or to response activities (early and late information processing activities, respectively). According to Wickens et al. (17), the Sternberg task can provide a precise estimate of mental workload since performance on this task has been described by a well-validated model of human information processing (34). For Experiments III and IV, differences in performance on the Sternberg task during the hold and the approach phases of flight as well as between single task and dual task conditions clearly indicated that the Sternberg task served as a secondary task. The increase in reaction time for the more difficult approach phase when compared to the hold phase is evidence that resources are being diverted from the Sternberg task to meet the increasing demands of the primary task. The similar increase in Sternberg task reaction time in the dual task condition was expected since the dual task requires dividing resources between the primary and secondary task. Thus, the Sternberg task appears to be useful in assessing differential workload situations. Despite the finding of a significant antiemetic drug effect on the primary task, however, the drugs failed to produce a main effect on the Sternberg task; nevertheless, the significant treatment x flight interaction indicates that the Sternberg task is affected in some way by antiemetic drugs

(see Appendix D). The results from Experiment IV indicate that measured mean values of 0.12% BAL also failed to produce a significant performance decrement on the Sternberg task, but a significant treatment effect was found for the primary task. Taylor et al. (22) reported similar results obtained in an earlier study performed in our laboratory which was concerned with the effect of atropine sulfate on pilot performance. In discussing the results, we hypothesized that atropine sulfate failed to affect cognitive processes involved in the performance of the Sternberg task, but affected the flight task. A similar hypothesis is also advanced to account for the antiemetic drug effects and the alcohol effects on the primary but not the Sternberg task. The Sternberg task and the flight task differ in terms of task difficulty, modality of stimulus input, mode of central processing (verbal vs. spatial) and complexity of response. From the data collected during these 3 experiments, however, we have not been able to determine the precise differences in information processing characteristics that prevented the Sternberg task from being affected by either atropine sulfate, antiemetic drugs, or by a high BAL, while flight performance was significantly degraded by each of these toxicants. A planned study which will examine the Sternberg task and the flight task as a single task and in a dual task condition may provide data to further examine the information processes involved.

The expected difference in reaction time between MSET 2 and 4 for the Sternberg task was not found in either Experiment III or IV during the dual condition, but MSET was significant for the single task for both experiments. Further analysis of the dual task indicated that MSET was significant for the hit (true), but not the correct rejection (false) for Experiments III and IV. A greater difference than expected was found for response type (hit vs. correct rejection). An earlier study indicated similar findings (22). Wickens et al. (17) reported that the larger effect was due in part to the differences in the backward movement required for the toggle switch for the correct rejection response.

We conducted Experiment IV to provide a reference for evaluating the relative performance decrement caused by the combination of antiemetic drugs. The results showed a significant treatment (BAL) main effect for the primary task which indicated that ethanol produced a decrement in pilot simulator instrument flight performance. The results are consistent with the findings of other investigators (10,11). Further analysis indicated that primary task variable decrement was due to the high BAL condition, (i.e., the measured 0.12% mean BAL). In comparing the performance decrements for the high BAL condition with the decrements that resulted from the PTC combination, we found that a significant effect was obtained for 3 primary task dependent variables for the PTC condition, while all 6 variables were affected by the high BAL condition. The percentage decrement in performance between the control and the PTC combination, and between the control and the high BAL was examined for each primary task dependent variable. For all variables, except for the LOC variable, the percentage performance decrement for the high BAL condition was greater than the decrement for the PTC combination. For the LOC variable, this relation was reversed. These data clearly indicate that the measured 0.12% mean BAL produced a relatively larger performance decrement than the PTC combination.

We interpret the finding that PTC produced a larger decrement on the LOC variable than that found for the high BAL condition as an indication of

differential resource allocation. Although analyzed as separate dependent variables, the LOC and GLS variables are part of a two-dimensional tracking task. The ILLIMAC simulator is very stable in pitch control which is used for GLS tracking, but not as stable in roll control which is used for LOC tracking. So, in the ILLIMAC simulator, LOC tracking is more difficult than GLS tracking. It appears that for the high BAL condition the subjects allocated a relatively higher percentage of resources to LOC tracking than to GLS tracking. The GLS, which has not been a sensitive indicator of drug effects, had a higher performance decrement than the LOC for the high vs. zero BAL conditions. The expected allocation of resources between the LOC and GLS, however, was found for the PTC condition. The time course of the effects of ethanol on primary task performance is also different from the PTC drug combination. The effects of PTC on performance were not seen until the final 3 flights, but the effects of ethanol were observed for the last 4 flights. The effects of ethanol appeared at 1:15 h postingestion compared to 1:55 h postingestion for the PTC drug combination.

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APPENDIX A

ALCOHOL ANOVAS (EXPERIMENT I), USING ALL SUBJECTS ON PRIMARY VARIABLES NUMBER OF OBSERVATIONS IN DATA SET = 156

General Linear Models Procedures SAS

Dependent Variable: LGALT1

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	87	45.77228554	9.23	0.0001	0.921947
Error	68	3.87511151	Root MSE		
Corrected Total	155	49.64739704	0.23871936		

Source	DF	SS	F Value	PR>F
Subject (Group)	4	11.57833429	50.79	0.0001
Treatment*Subject (Group)	12	3.97821492	5.82	0.0001
Flight*Subject (Group)	16	0.76378581	0.84	0.6397
Experimental Session*Flight	12	0.98226865	1.44	0.1713
Treatment*Flight	12	0.34092076	0.50	0.9086

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.06968274	0.36	0.8300
Flight*Group	12	0.42544367	0.74	0.6951

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	3	22.32823218	2.57	0.1919

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	0.28203903	0.28	0.8363
Treatment	3	3.42354187	3.44	0.0518

Note: LGALT1 = Log RMS Altitude while straight and level.

Dependent Variable: LGALT2

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	87	48.69820324	10.82	0.0001	0.932624
Error	68	3.51811799	Root MSE		
Corrected	155	52.21632123	0.22745775		

Source	DF	SS	F Value	PR>F
Subject (Group)	4	15.33601864	74.11	0.0001
Treatment*Subject (Group)	12	3.80882326	6.13	0.0001
Flight*Subject (Group)	16	0.54970093	0.66	0.8183
Experimental Session*Flight	12	0.42116261	0.68	0.7661
Treatment*Flight	12	0.23603190	0.38	0.9663

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.53975498	3.93	0.0209
Flight*Group	12	0.29652915	0.72	0.7148

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	3	20.80725720	1.81	0.2852

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	0.25046253	0.26	0.8507
Treatment	3	4.78249802	5.02	0.0175

Note: LGALT2 = Log RMS Altitude while turning.

Dependent Variable: LGGS

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	87	15.18880970	1.69	0.0122	0.684347
Error	68	7.00578830	Root MSE		
Corrected Total	155	22.19459800	0.32097710		

Source	DF	SS	F Value	PR>F
Subject (Group)	4	1.84153128	4.47	0.0029
Treatment*Subject (Group)	12	1.51561596	1.23	0.2841
Flight*Subject (Group)	16	1.69981911	1.03	0.4367
Experimental Session*Flight	12	2.37396462	1.92	0.0469
Treatment*Flight	12	0.86008717	0.70	0.7500

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	1.32127902	3.11	0.0452
Flight*Group	12	2.17988666	1.71	0.1567

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	0.26726098	0.71	0.5670
Treatment	3	1.73908342	4.59	0.0232

Note: LGGS = Log RMS Glide Slope.

Dependent Variable: LGLOC

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	87	17.05031629	2.75	0.0001	0.778528
Error	68	4.85039662		Root MSE	
Corrected Total	155	21.90071291		0.26707557	

Source	DF	SS	F Value	PR>F
Subject (Group)	4	4.13400433	14.49	0.0001
Treatment*Subject (Group)	12	3.41764480	3.99	0.0001
Flight*Subject (Group)	16	0.81842847	0.72	0.7672
Experimental Session*Flight	12	0.26556855	0.31	0.9854
Treatment*Flight	12	0.50375286	0.59	0.8440

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.20875608	1.02	0.4265
Flight*Group	12	0.63683344	1.04	0.4630

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	3	4.33819178	1.40	0.3654

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	0.33111834	0.39	0.7640
Treatment	3	1.63807865	1.92	0.1807

Note: LGLOC = Log RMS Localizer.

APPENDIX B

ANTIEMETIC ANOVAS (EXPERIMENT II), USING ALL SUBJECTS ON PRIMARY VARIABLES NUMBER OF OBSERVATIONS IN DATA SET = 314

General Linear Models Procedure SAS

Dependent Variable: LGALT1

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	151	74.72128445	10.58	0.0001	0.907942
Error	162	7.57611883		Root MSE	
Corrected Total	313	82.29740329		0.21625486	

Source	DF	SS	F Value	PR>F
Subject (Group)	12	47.27940268	84.25	0.0001
Drug*Subject (Group)	36	3.43157252	2.04	0.0014
Flight*Subject (Group)	48	2.99412639	1.33	0.0952
Experimental Session*Flight	12	0.89994350	1.60	0.0951
Drug*Flight	12	0.77606455	1.38	0.1788

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.26947249	1.08	0.3769
Flight*Group	12	0.72843513	0.97	0.4868

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	3	14.86342018	1.26	0.3327

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	0.36965632	1.29	0.2918
Drug	3	1.17702221	4.12	0.0131

Note: LGALT1 = Log RMS Altitude while straight and level.

Dependent Variable: LGALT2

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	151	86.22911203	10.73	0.0001	0.909066
Error	162	8.62553604		Root MSE	
Corrected Total	313	94.85464806		0.23074672	

Source	DF	SS	F Value	PR>F
Subject (Group)	12	59.97788489	93.87	0.0001
Drug*Subject (Group)	36	4.08619635	2.13	0.0007
Flight*Subject (Group)	48	3.55623274	1.39	0.0667
Experimental Session*Flight	12	0.57759618	0.90	0.5444
Drug*Flight	12	0.98128269	1.54	0.1161

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.28325443	0.96	0.4403
Flight*Group	12	0.78277099	0.88	0.5717

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	3	12.79292480	0.85	0.4914

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	0.44572445	1.31	0.2865
Drug	3	0.80051770	2.35	0.0886

Note: LGALT2 = Log RMS Altitude while turning.

Dependent Variable: LGGS

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	151	37.40353655	3.44	0.0001	0.762070
Error	162	11.67795951		Root MSE	
Corrected total	313	49.08149605		0.26848868	

Source	DF	SS	F Value	PR>F
Subject (Group)	12	20.88101195	24.14	0.0001
Drug*Subject (Group)	36	5.05448150	1.95	0.0027
Flight*Subject (Group)	48	2.73450587	0.79	0.8279
Experimental Session*Flight	12	0.75059895	0.87	0.5810
Drug*Flight	12	1.04383647	1.21	0.2825

Tests of the hypotheses using MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.32925900	1.44	0.2338
Flight*Group	12	1.12262611	1.64	0.1114

Tests of the hypotheses using MS for Subject (Group) as an error term

Source	DF	SS	F-Value	PR>F
Group	3	4.29214103	0.82	0.5064

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F-Value	PR>F
Experimental Session	3	0.51368565	1.22	0.3166
Drug	3	1.09841524	2.61	0.0665

Note: LGGS = Log RMS Glide Slope

Dependent Variable: LGLOC

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	151	45.70958486	4.94	0.0001	0.821625
Error	162	9.92358968	Root MSE		
Corrected Total	313	55.63317454	0.24750096		

Source	DF	SS	F Value	PR>F
Subject (Group)	12	27.05374699	36.80	0.0001
Drug*Subject (Group)	36	2.87353544	1.30	0.1365
Flight*Subject (Group)	48	4.72165033	1.61	0.0155
Experimental Session*Flight	12	0.88730531	1.21	0.2822
Drug*Flight	12	0.72212979	0.98	0.4679

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.25579708	0.65	0.6296
Flight*Group	12	0.95346132	0.81	0.6410

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	3	2.86334956	0.42	0.7397

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	3	1.88175198	7.86	0.0004
Drug	3	1.94442946	8.12	0.0003

Note: LGLOC = Log RMS Localizer

APPENDIX C

COMBINATION ANTIEMETIC ANOVAS (EXPERIMENT III), USING ALL SUBJECTS ON PRIMARY VARIABLES
NUMBER OF OBSERVATIONS IN DATA SET = 179

General Linear Models Procedures SAS

Dependent Variable: LGALT1

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	10.69483467	6.26	0.0001	0.886918
Error	79	1.36359218		Root MSE	
Corrected Total	178	12.05842685		0.13137983	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	4.44461934	28.61	0.000
Experimental Session*Flight	8	0.16483038	1.19	0.313
Drug*Flight	8	0.33281941	2.41	0.022
Flight*Subject (Group)	36	0.66859852	1.08	0.384
Drug*Subject (Group)	18	2.42613019	7.81	0.000

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.36345801	4.89	0.0030
Flight*Group	8	0.07116407	0.48	0.8629

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	1.46432411	1.48	0.2776

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.01657207	0.06	0.9406
Drug	2	0.14503603	0.54	0.5930
Drug*Group	2	0.46110430	1.71	0.2089

Note: LGALT1 = Log RMS Altitude while straight and level.

Dependent Variable: LGALT2

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	8.57266657	3.31	0.0001	0.805714
Error	79	2.06717233		Root MSE	
Corrected Total	178	10.63983890		0.16176136	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	4.00635960	17.01	0.000
Experimental Session*Flight	8	0.23406263	1.12	0.360
Drug*Flight	8	0.49701655	2.37	0.024
Flight*Subject (Group)	36	0.72711534	0.77	0.803
Drug*Subject (Group)	18	1.13752366	2.42	0.003

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.64649808	8.00	0.0001
Flight*Group	8	0.28107121	1.74	0.1227

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.75455690	0.85	0.4600

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.01117254	0.09	0.9158
Drug	2	0.23765157	1.88	0.1813
Drug*Group	2	0.03712521	0.29	0.7490

Note: LGALT2 = Log RMS Altitude while turning.

Dependent Variable: LGTC1

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	4.65783420	6.32	0.0001	0.887896
Error	79	0.58808648	Root MSE		
Corrected total	178	5.24592067	0.08627939		

Source	DF	SS	F Value	PR>F
Subject (Group)	9	2.12679719	31.74	0.000
Experimental Session*Flight	8	0.04681752	0.79	0.616
Drug*Flight	8	0.23056499	3.87	0.000
Flight*Subject (Group)	36	0.38970872	1.45	0.084
Drug*Subject (Group)	18	0.30624760	2.29	0.006

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.15724932	3.63	0.0138
Flight*Group	8	0.10198059	1.18	0.3392

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.85776755	1.81	0.2177

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.04151968	1.22	0.3185
Drug	2	0.25249501	7.42	0.0045
Drug*Group	2	0.10893722	3.20	0.0646

Note: LGTC1 = Log RMS Turn Coordinator while straight and level.

Dependent Variable: LGTC2

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	7.88919355	3.97	0.0001	0.832469
Error	79	1.58766785		Root MSE	
Corrected Total	178	9.47686140		0.14176410	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	4.72298433	26.11	0.000
Experimental Session*Flight	8	0.10057983	0.63	0.753
Drug*Flight	8	0.03772867	0.23	0.983
Flight*Subject (Group)	36	0.56043700	0.77	0.800
Drug*Subject (Group)	18	0.44743991	1.24	0.253

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.99448353	15.97	0.0001
Flight*Group	8	0.19571848	1.57	0.1680

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.39252322	0.37	0.6982

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.01366417	0.27	0.7628
Drug	2	0.28109811	5.65	0.0124
Drug*Group	2	0.09714172	1.95	0.1706

Note: LGTC2 = Log RMS Turn Coordinator while turning.

Dependent Variable: LGLOC

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	28.73606297	3.04	0.0001	0.792078
Error	79	7.54328779		Root MSE	
Corrected Total	178	36.27935075		0.30900592	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	10.66960469	12.42	0.000
Experimental Session*Flight	8	1.75821009	2.30	0.028
Drug*Flight	8	2.26100304	2.96	0.006
Flight*Subject (Group)	36	3.35850658	0.98	0.518
Drug*Subject (Group)	18	2.71995380	1.58	0.085

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	1.04900213	2.81	0.0396
Flight*Group	8	0.97597353	1.31	0.2709

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.15595764	0.07	0.9368

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.13779313	0.46	0.6410
Drug	2	5.53880052	18.33	0.0001
Drug*Group	2	0.06740685	0.22	0.8023

Note: LGLOC = Log RMS Localizer.

Dependent Variable: LGGS

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	30.01178946	3.63	0.0001	0.819889
Error	79	6.59291323		Root MSE	
Corrected Total	178	36.60470269		0.28888509	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	15.91990498	21.20	0.000
Experimental Session*Flight	8	1.10435671	1.65	0.123
Drug*Flight	8	1.20432026	1.80	0.088
Flight*Subject (Group)	36	2.75184199	0.92	0.606
Drug*Subject (Group)	18	3.81879473	2.54	0.002

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	1.38765806	4.54	0.0045
Flight*Group	8	0.43067645	0.70	0.6857

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	1.73231134	0.49	0.6283

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.71168559	1.68	0.2148
Drug	2	0.35395241	0.08	0.9203
Drug*Group	2	0.73853464	1.74	0.2037

Note: LGGS = Log RMS Glide Slope.

APPENDIX D

COMBINATION ANTIEMETIC ANOVA (EXPERIMENT III), USING REACTION TIME ON STERNBERG TASK (DUAL CONDITION) FOR 12 SUBJECTS NUMBER OF OBSERVATIONS IN DATA SET = 1432

General Linear Models Procedures SAS

Dependent Variable: RT

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	112	136.67429533	22.74	0.0001	0.670602
Error	1251	67.13410851		Root MSE	
Corrected Total	1363	203.80840383		0.23165568	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	99.74483414	206.52	0.000
HA (Hold-Approach)	1	1.80773199	33.69	0.000
TF (True-False)	1	17.34816647	323.27	0.000
MSET	1	0.14478141	2.70	0.100
TF*MSET	1	0.29487139	5.49	0.019
MSET*HA	1	0.00615792	0.11	0.734
TF*HA	1	0.12185592	2.27	0.132
TF*MSET*HA	1	0.04923540	0.92	0.338
Group*MSET	2	0.00616707	0.06	0.944
Group*TF	2	0.07967424	0.74	0.476
Group*HA	2	0.58918772	5.49	0.004
Flight*Subject (Group)	36	1.91846311	0.99	0.481
Drug*Subject (Group)	18	1.84506088	1.91	0.012
Experimental Session*Flight	8	0.82425314	1.92	0.053
Drug*Flight	8	1.43345239	3.34	0.000

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	2.24225915	10.52	0.0001
Flight*Group	8	0.34486466	0.81	0.5992

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	8.06792896	0.36	0.7047

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	1.28152721	6.20	0.0090
Drug	2	0.44325102	2.16	0.1440
Drug*Group	2	0.03154027	0.15	0.8585

Note: RT = Reaction Time

APPENDIX E

COMBINATION ANTIEMETIC ANOVA (EXPERIMENT IV), USING REACTION TIME ON STERNBERG SINGLE TASK FOR 12 SUBJECTS
NUMBER OF OBSERVATIONS IN DATA SET = 568

General Linear Models Procedures SAS

Dependent Variable: RT

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	90	38.15801147	36.14	0.0001	0.872092
Error	477	5.59657404	Root MSE		
Corrected	567	43.75458551	0.10831833		

Source	DF	SS	F Value	PR>F
Subject (Group)	9	26.67549949	252.62	0.000
TF (True-False)	1	4.19932144	357.91	0.000
MSET	1	0.23593105	20.11	0.000
TF*MSET	1	0.01906981	1.63	0.203
Group*MSET	2	0.06450158	2.75	0.065
Group*TF	2	0.02785104	1.19	0.306
Flight*Subject (Group)	27	0.39759574	1.26	0.178
Drug*Subject (Group)	18	1.02684905	4.86	0.000
Experimental Session*Flight	6	0.16111030	2.29	0.034
Drug*Flight	6	0.76203226	10.82	0.000

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	3	0.64871156	14.68	0.0001
Flight*Group	6	0.11482125	1.30	0.2910

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	2.73712821	0.46	0.6443

Tests of hypotheses using the MS for Drug*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.44163282	3.91	0.0390
Drug	2	0.26669470	2.34	0.1252
Drug*Group	2	0.05364242	0.47	0.6324

Note: RT = Reaction Time.

APPENDIX F

ALCOHOL ANOVAS (EXPERIMENT IV), USING ALL SUBJECTS ON PRIMARY VARIABLES NUMBER OF OBSERVATIONS IN DATA SET = 179

General Linear Models Procedures SAS

Dependent Variable: LGALT1

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	16.00304290	4.50	0.0001	0.852582
Error	77	2.76705919		Root MSE	
Corrected Total	176	18.77010209		0.18956749	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	8.98333659	27.78	0.000
Experimental Session*Flight	8	0.18748308	0.65	0.731
Treatment*Flight	8	0.12505271	0.43	0.896
Flight*Subject (Group)	36	1.25981789	0.97	0.523
Treatment*Subject (Group)	18	1.26693512	1.96	0.022

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.13907922	0.99	0.4236
Flight*Group	8	0.29304179	1.05	0.4207

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	2.39852912	1.20	0.3448

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.22692296	1.61	0.2270
Treatment	2	0.79487203	5.65	0.0125
Treatment*Group	2	0.00626808	0.04	0.9566

Note: LGALT1 = Log RMS Altitude while straight and level.

Dependent Variable: LGALT2

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	21.65896388	5.26	0.0001	0.871221
Error	77	3.20149812		Root MSE	
Corrected Total	176	24.86046200		0.20390659	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	12.30412130	32.88	0.000
Experimental Session*Flight	8	0.03468338	0.10	0.999
Treatment*Flight	8	0.31656524	0.95	0.479
Flight*Subject (Group)	36	1.63062347	1.09	0.369
Treatment*Subject (Group)	18	2.23268937	2.98	0.000

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.27543802	1.52	0.2169
Flight*Group	8	0.39344597	1.09	0.3950

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	1.98912343	0.73	0.5095

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.06076004	0.24	0.7853
Treatment	2	1.78002709	7.18	0.0051
Treatment*Group	2	0.01646119	0.07	0.9360

Note: LGALT2 = Log RMS Altitude while turning.

Dependent Variable: LGTC1

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	3.22826377	4.22	0.0001	0.844344
Error	77	0.59513567		Root MSE	
Corrected total	176	3.82339943		0.08791493	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	0.70864139	10.19	0.000
Experimental Session*Flight	8	0.09486551	1.53	0.159
Treatment*Flight	8	0.20015153	3.24	0.003
Flight*Subject (Group)	36	0.57993243	2.08	0.003
Treatment*Subject (Group)	18	0.51426205	3.70	0.000

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.08038540	1.25	0.3085
Flight*Group	8	0.07861445	0.61	0.7634

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.37958676	2.41	0.1451

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.00288302	0.05	0.9509
Treatment	2	0.55548563	9.72	0.0014
Treatment*Group	2	0.01463070	0.26	0.7769

Note: LGTC1 = Log RMS Turn Coordinator while straight and level.

Dependent Variable: LGTC2

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	9.13486177	3.43	0.0001	0.815295
Error	77	2.06950772		Root MSE	
Corrected Total	176	11.20436949		0.16394122	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	3.36277293	13.90	0.000
Experimental Session*Flight	8	0.09501360	0.44	0.892
Treatment*Flight	8	0.29559553	1.37	0.221
Flight*Subject (Group)	36	1.09775050	1.13	0.316
Treatment*Subject (Group)	18	0.99030378	2.05	0.016

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.34917386	2.86	0.0371
Flight*Group	8	0.27461662	1.13	0.3699

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.03823684	0.05	0.9504

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.04220785	0.38	0.6868
Treatment	2	1.87353603	17.03	0.0001
Treatment*Group	2	0.36527231	3.32	0.0593

Note: LGTC2 = Log RMS Turn Coordinator while turning.

Dependent Variable: LGLOC

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	52.78453342	3.17	0.0001	0.803053
Error	77	12.94532288		Root MSE	
Corrected Total	176	65.72985631		0.41002570	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	31.07323440	20.54	0.000
Experimental Session*Flight	8	0.66560634	0.49	0.856
Treatment*Flight	8	1.24282679	0.92	0.501
Flight*Subject (Group)	36	7.68233896	1.27	0.190
Treatment*Subject (Group)	18	3.21020512	1.06	0.406

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.57957636	0.68	0.6110
Flight*Group	8	2.44064732	1.43	0.2179

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.46064475	0.07	0.9359

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.03818112	0.11	0.8991
Treatment	2	3.49533714	9.80	0.0013
Treatment*Group	2	0.00835353	0.02	0.9769

Note: LGLOC = Log RMS Localizer.

Dependent Variable: LGGS

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	99	33.47847119	4.02	0.0001	0.837863
Error	77	6.47849160		Root MSE	
Corrected Total	176	39.95696279		0.29006250	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	17.92834294	23.68	0.000
Experimental Session*Flight	8	0.92192716	1.37	0.223
Treatment*Flight	8	0.72502849	1.08	0.388
Flight*Subject (Group)	36	4.50793138	1.49	0.073
Treatment*Subject (Group)	18	1.75316886	1.16	0.317

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.31776494	0.63	0.6412
Flight*Group	8	1.76616561	1.76	0.1173

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	1.89043544	0.47	0.6369

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.18911328	0.97	0.3977
Treatment	2	2.54790880	13.08	0.0003
Treatment*Group	2	0.60563504	3.11	0.0692

Note: LGGS = Log RMS Glide Slope.

APPENDIX G

ALCOHOL ANOVA (EXPERIMENT IV), USING REACTION TIME ON STERNBERG TASK (DUAL CONDITION) FOR 12 SUBJECTS NUMBER OF OBSERVATIONS IN DATA SET = 1373

General Linear Models Procedures SAS

Dependent Variable: RT

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	112	105.16044946	18.02	0.0001	0.615607
Error	1260	65.66359009		Root MSE	
Corrected Total	1372	170.82403955		0.22828482	

Source	DF	SS	F Value	PR>F
Subject (Group)	9	68.77612038	146.64	0.000
HA (Hold-Approach)	1	1.87155087	35.91	0.000
TF (True-False)	1	14.69717209	282.02	0.000
MSET	1	0.07035735	1.35	0.245
TF*MSET	1	0.03410550	0.65	0.418
MSET*HA	1	0.14251262	2.73	0.098
TF*HA	1	0.03765224	0.72	0.395
TF*MSET*HA	1	0.10699544	2.05	0.152
Group*MSET	2	0.05234662	0.50	0.605
Group*TF	2	1.44331018	13.85	0.000
Group*HA	2	0.18504088	1.78	0.169
Flight*Subject (Group)	36	2.42557290	1.29	0.116
Treatment*Subject (Group)	18	4.92252041	5.25	0.000
Experimental Session*Flight	8	0.26142354	0.63	0.755
Treatment*Flight	8	1.03016731	2.47	0.011

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	4	0.79256091	2.94	0.0335
Flight*Group	8	1.04477530	1.94	0.0840

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	6.89795598	0.45	0.6504

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.29920223	0.54	0.5919
Treatment	2	0.25518206	0.47	0.6345
Treatment*Group	2	0.07518495	0.14	0.8725

Note: RT = Reaction Time

APPENDIX H

ALCOHOL ANOVA (EXPERIMENT IV), USING REACTION TIME ON STERNBERG SINGLE TASK FOR 12 SUBJECTS NUMBER OF OBSERVATIONS IN DATA SET = 572

General Linear Models Procedures SAS

Dependent Variable: RT

Source	DF	Sum of Squares	F Value	PR>F	R-Square
Model	90	31.10368144	31.41	0.0001	0.854590
Error	481	5.29232835	Root MSE		
Corrected	571	36.39600979	0.10489405		

Source	DF	SS	F Value	PR>F
Subject (Group)	9	21.14317786	213.51	0.000
TF (True-False)	1	3.37785963	307.00	0.000
MSET	1	0.37818715	34.37	0.000
TF*MSET	1	0.03497853	3.18	0.075
Group*MSET	2	0.00912940	0.41	0.660
Group*TF	2	0.07501353	3.41	0.033
Flight*Subject (Group)	27	0.81968024	2.76	0.000
Treatment*Subject (Group)	18	2.98386847	15.07	0.000
Experimental Session*Flight	6	0.40164247	6.08	0.000
Treatment*Flight	6	0.12862092	1.95	0.071

Tests of hypotheses using the MS for Flight*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Flight	3	0.41215473	4.53	0.0107
Flight*Group	6	0.41065225	2.25	0.0682

Tests of hypotheses using the MS for Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Group	2	0.11677235	0.02	0.9755

Tests of hypotheses using the MS for Treatment*Subject (Group) as an error term

Source	DF	SS	F Value	PR>F
Experimental Session	2	0.32805756	1.00	0.3891
Treatment	2	0.29245000	0.88	0.4311
Treatment*Group	2	0.01441015	0.04	0.9576

Note: RT = Reaction Time.